

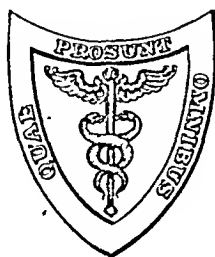


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OSTEOGENESIS IMPERFECTA (SO-CALLED FRAGILITAS  
OSSIUM).

BY P. WILLIAM NATHAN, M.D.,  
OF NEW YORK CITY.

ACCORDING to Ballentyne<sup>1</sup> our knowledge of the systemic bone diseases of the foetus is so deficient that for the present a proper classification is impossible. For this reason he considers it better to make no attempt at all to group these cases, but prefers to arrange the various instances of fetal bone disease which have come under his own observation under individual types, designating each by a letter of the alphabet.

But, even were our knowledge of these diseases so deficient as Ballentyne would have us believe, such a grouping of the cases would only make the matter more confusing, and its general adoption would prove extremely unsatisfactory. Fortunately, such a course is entirely unnecessary, for the pathological anatomy of fetal bone disease has been carefully studied by competent observers, and the lesions which have been found are so characteristic that the classification is a comparatively easy matter.

Thus, the disease formerly known as congenital or fetal rachitis has been carefully studied by a number of authors, and has been found to be a distinct systemic bone disease, having nothing in common with rachitis. Kaufman showed conclusively that this affection may be represented by cases which apparently differ decidedly from one another, but which, nevertheless, are identical in the principal features. Two such variations are recorded by Ballentyne as types C and D.

In a recent paper<sup>2</sup> on this subject I showed that this disease is

<sup>1</sup> The Pathology and Hygiene of the Foetus.

<sup>2</sup> Nathan, Chondrodystrophia Foetalis, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, April, 1904, p. 690.

not nearly so fatal as had been previously believed. The number of isolated living cases recorded in the literature, and the number of living examples seen by Kassowitz and myself, show that not infrequently the foetus survives, and that after birth and during the subsequent life these individuals present characteristic and easily recognized peculiarities. So that in chondrodystrophia foetalis we have a fetal systemic bone disease which has not alone a well-understood pathological anatomy but also characteristic clinical features.

Under types A and B, Ballentyne records two cases of fetal bone disease which have all the characteristic lesions of a disease long known as osteogenesis imperfecta. Quite a number of cases of this malady have been recognized and described since Berdenave published the first case in 1763. The name was given it by Vrolik. The pathology has been studied and accurately described by a number of writers, particularly by Stilling, Hildebrand, and Buday, who have demonstrated that the lesions are characteristic and easily differentiated from those of other diseases.

Thus, Ballentyne's cases, recorded as types, are not really types of distinct bone diseases at all, but simply represent cases of two well-understood pathological conditions. Moreover, all the cases of systemic bone diseases in the foetus, if we except those associated with some general constitutional anomaly (cretinism or syphilis) have been found to be cases of either chondrodystrophia foetalis or osteogenesis imperfecta. As these two diseases present peculiarities, both in their pathology and in their external characteristics, which are not alone distinct, but in absolute contradistinction to each other, a sound and adequate classification, far from being impossible, is really a simple matter.

The systemic bone diseases of the foetus may therefore be divided into three classes: 1, those associated with other constitutional anomalies; 2, chondrodystrophia foetalis; 3, osteogenesis imperfecta.

The last, which is to be discussed in this paper, has been fairly well known to pathologists for some time; but, as the cases reported under this name were practically all confined to stillborn or premature infants, it has not, up to the present time, been recognized or studied by the clinician. At any rate, so far as I can ascertain, no case in the living subject has been reported under the name of osteogenesis imperfecta.

The facilities accorded me by my friend and chief, Dr. W. R. Townsend, at the "Hospital for the Ruptured and Crippled," have enabled me to examine clinically many cases of congenital bone disease. Among the numerous and diverse abnormalities which have appeared at the "out-door department" of the hospital during the past five years I was much surprised to find two cases which, from their history and clinical manifestations, are undoubtedly cases of osteogenesis imperfecta.

As all those who have previously written upon this subject were quite positive that this disease is incompatible with extra-uterine life, I should have hesitated to class these cases as such had it not been for the fact that the clinical manifestations at birth and during early life were exactly like those found in stillborn infants with osteogenesis imperfecta. Moreover, the symptoms later on in life were exactly those which a study of the pathology of this disease would lead us to anticipate.

In order to show the connection between the pathological anatomy and the clinical manifestations of this disease, I will give a brief summary of the pathology.

The general appearance of the newborn infant or foetus with osteogenesis imperfecta is peculiar. It resembles somewhat the chondrodystrophic individual; but this resemblance is only superficial and confined entirely to thickened skin and subcutaneous tissues which give these individuals an obese or oedematous appearance. However, the skin and subderma in osteogenesis imperfecta are not nearly so uniformly affected as in chondrodystrophia, for there are many cases in which these are perfectly normal. In osteogenesis imperfecta the extremities are not shortened, at any rate, not as a result of cessation or retardation of growth. They are, however, often much bent and deformed, and they are always so brittle that the slightest violence results in fracture. Not infrequently there are intrauterine fractures. These may be recent and present the ordinary signs of fracture, or they may be firmly united and only evident by the abundant calluses present. The latter may be so numerous that they give the bone a peculiar nodular appearance. The intrauterine fractures may cause much deformation, but they unite firmly, as a rule, and pseudarthrosis is rare.

On examining the body more closely it is found that the fragility of the bones is not confined to the extremities, but extends to all the bones of the body. Thus, the spinal column is soft and friable, presenting anteroposterior or lateral deviations; the ribs are often fractured, sometimes to an extraordinary extent, as in Merkel's case, which presented forty-three fractures of the ribs alone. The clavicle is often fractured or shows signs of intrauterine fracture and repair. In fact, the stability of the entire skeleton is more or less markedly diminished, and, instead of acting as a framework for the body, is its most delicate and fragile part. Not alone is this true of the skeleton of the body, but it is also true of the cranial vault. Here ossification is always defective, though sometimes this is only evident by the widely patent sutures; occasionally it is entirely absent, and the cranial vault consists simply of a soft membranous sac.

The examination of the bones after their removal from the body shows changes which correspond with those found in the parts accessible externally. The bones are delicate and fragile, and the



most insignificant force is sufficient to cause fracture. At times the periosteal bone shell is so thin that it can be crushed between the fingers.

Sections of the bones show them to be exceedingly porous. The trabeculae are thin and defective; the outer periosteal layer is thin, and, instead of being composed of a continuous dense bone, consists of small bone plates or trabeculae. Calcification of the osteoid tissue is defective, and in some places absent entirely. The epiphyseal cartilages are normal as to size and consistence.

Microscopic examination shows that the pathological process is confined entirely to the shaft of the bone, where it seems to prevent the normal development and calcification of the osteoid tissue. The growth of the cartilage—that is, the proliferation of the cells—the formation of rows and their subsequent calcification and disintegration go on in a perfectly normal manner; only when the stage of true bone formation is reached are there evidences of disease. The osteoblasts are diminished in numbers; they deposit only a thin layer of osteoid tissue, and calcification is retarded, deficient, or entirely absent. The organs of the body, aside from the bones, are apparently perfectly normal.

Osteogenesis imperfecta, therefore, is a systemic bone disease which evidently attacks the very young foetus, and, without causing other appreciable abnormalities, prevents or disturbs the normal development and calcification of the osteoid tissue. Externally the disease manifests itself by defective development of the cranial vault and fragility of the bones of the entire skeleton.

The general opinion (Schmidt, Ballentyne, Schuchardt, and others) has been that the foetus with osteogenesis imperfecta practically always dies during intrauterine life. So far in all the cases reported the newborn infant was either dead or died within a short time afterward. I am, however, in a position to say that this is not nearly always the case. The cases which I am about to record presented exactly the manifestations which are pathognomonic of osteogenesis imperfecta at birth, and yet both have survived and are still living. In fact, I believe and I hope to prove that these are not the only living examples of this disease. Before, however, proceeding to discuss this point, I will give the histories of my cases.

CASE I.—H. M., aged sixteen months. First seen on June 17, 1901.

*Family History.* Parents both apparently healthy, and there is no chronic constitutional or mental disease in the family. The father is said to be addicted to drink, but not excessively so, nor does dipsomania occur in his family.

During the early months of pregnancy the mother resorted to various expedients (drugs) to induce abortion, but otherwise the pregnancy was normal and the infant was carried to full term. The head presented and the labor was uneventful.

From the first it was noticed that the infant was peculiar; it appeared obese, and the head was large. Moreover, the lower extremities assumed a very remarkable attitude, which they maintained for some time after birth, and even to-day there is a tendency to keep the limbs in this position. (Fig. 1.) The thighs were flexed at maximum and rotated out; the legs were flexed to a right angle and closely approximated the abdomen, the outer edge of the left foot lying upon the inner surface of the right leg, and the outer edge of the right foot lying upon the inner surface of the left leg. At birth the child was very weak, but it nursed without apparent difficulty, and soon improved, so that by the end of the third month it was doing fairly well. At this time the mother discontinued

FIG. 1.



nursing and began to feed the infant various proprietary foods. None of the foods seemed to agree, and the child steadily declined until it came under my observation.

*Status.* Very delicate male infant, aged sixteen months, having the peculiar appearance shown in Fig. 2. The head is large, the fontanelles, both anterior and posterior, are widely open. All the cranial sutures are patent and can be readily felt. The frontal suture is patent and extends half-way down the forehead. The two lower incisors are just coming through.

The thorax is prominent, somewhat barrel-shaped, but there is no abnormal breaking of the ribs. The abdomen is protruding, and there is double inguinal hernia.

The extremities, both upper and lower, are much bent and deformed. There is angular deformity, evidently the result of

fracture, of the left radius. Both femora are bowed anteriorly, and the legs present both anterior and lateral deviations. The anterior bending of the lower ends of the tibiæ is angular, and in appearance is very much like the deformity which occurs in the same situation as a result of infraction in rachitic children. There is lumbar kyphosis of the spine.

The child was placed upon a diet, but as the nature of the condition was not suspected, nothing was said about careful handling. The general health soon improved.

FIG. 2



A few months after treatment was begun it was noticed that the child refused to use the right arm, and cried when it was handled. On examination it was found that the humerus was fractured. The mother denied that there had been any traumatism, and she did not know that it had been injured until the child refused to use the arm. The fracture healed perfectly within four weeks.

In August, 1901, at the earnest solicitation of the mother, and not realizing the condition of affairs, I undertook to correct the deformities of the legs. The child being anæsthetized, I proceeded

to attempt manual correction. However, I was greatly surprised to find that the bones fractured like cardboard as soon as I attempted to bend them. The force necessary to break the bones was insignificant, not nearly sufficient to fracture any but the most brittle bone. The fractures were put up in plaster of Paris, and union was firm at the end of four weeks.

Now that the fragility of the bones was apparent, I instructed the mother to protect the child from violence. However, though

FIG. 3.



these instructions were carefully followed, he began to have fractures at frequent intervals. The most insignificant force seemed to be sufficient to occasion fracture. Knocking the limb slightly against the side of his carriage or chair, grasping suddenly for some object, etc., have given rise to fractures of the arms or thighs. During the fall of 1901 he fractured his right humerus for the second time; in the summer of 1902 he fractured the left humerus; in the fall the right radius and ulna. During 1903, at various times,

he fractured the lower end of the right femur, the upper end of the left femur, and the lower end of the right tibia. In January of this year he fractured the upper end of the left femur.

The deformities present when he first came under observation, and the extreme fragility of the bones, which was noted at the time of his operation, make it more than probable that he had sustained fractures before I saw him. These were probably unnoticed at the time, which is not at all surprising, because the fractures were all attended by very little pain and inflammatory reaction. The number of fractures which have occurred cannot be positively ascertained. The mother cannot remember them all, and, as they live away from New York, I can only record those which have been verified by myself. Up to the present time (July, 1904) he has not had less than twelve fractures.

Aside from the fragility of the bones, the boy presents no other constitutional defect. He is intelligent, talks very well for his years, and the general health is good. The fontanelles and sutures are now closed, and his teeth are coming in. Fig. 3 shows the present appearance.

CASE II.—R. M., male, aged seventeen years. The father died of general paralysis. The mother, aged sixty-five years, is living and in good health. There are six brothers and sisters, who are all well. No constitutional disease in the ancestors, nor is there a history of any fragility of bones in the family.

He is the youngest child, and the father already showed the symptoms of general paralysis when he was born. The pregnancy and labor were uneventful. At birth he appeared plump, and, according to the mother, a very nice looking child. It was soon noticed, however, that the head was rather large and that it was remarkably soft, the cranial sutures being widely open, and the individual bones of the cranial vault were freely movable.

Evidently the physician in attendance noticed the peculiarity and weakness of the infant, for it was kept lying flat upon a pillow and handled with great caution. However, in spite of the great care exercised over it, the child grew weaker, and its life was despaired of.

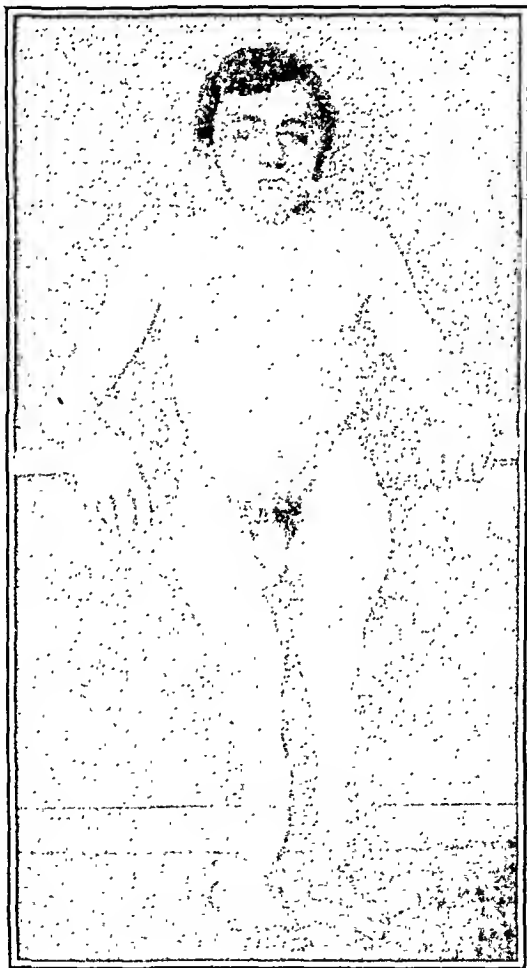
Three weeks after birth, while having the diaper changed, the right femur was fractured, and in spite of the fact that he continued to recline upon a pillow and was handled with extreme caution, he sustained three fractures during the first six months of his life. After the ninth month his general health began to improve, and since then he has enjoyed good health.

The fragility of the bones has, however, continued. According to the mother, he has sustained no less than thirty-five fractures. The bones of the extremities have all been fractured at one time or another, and he is said to have had two fractures at the same time. The earlier fractures occurred in spite of the most careful handling, and the later ones have all been due to insignificant violence.

It seems, however, that the fragility abated somewhat as he grew older, for he began to make some attempt to walk when he was six, and could get around by holding on to furniture or other assistance when he was eight years old. During this period he sustained numerous fractures, but later he was fitted with braces and learned to use crutches, and with their aid he now walks in some security. The last fracture occurred two years ago.

The earlier fractures were always treated by a physician; but later, as they grew more frequent, and as they were accompanied by very little pain or swelling, they were left to themselves. Union has always been firm.

FIG. 4.



His present condition is shown by Fig. 4, by which it is seen that all the bones present a remarkable series of deformities. He has a circumscribed spinal lordosis in the lower dorsal region. Besides the fragility of the bones, he shows absolutely no other abnormalities; his general health is good, and he is intelligent.

Had it not been for the fact that I saw my first case while he was still very young and still presented the signs of defective ossification of the cranial bones, I should, no doubt, have considered this a case of idiopathic fragilitas ossium. However, soon after I saw him I began to study the fetal bone diseases, and while so doing I was struck by the likeness between this and the cases of osteogenesis imperfecta. In studying the case more carefully and comparing it with both osteogenesis imperfecta and fragilitas ossium, I became convinced that not only this case but the majority of cases of so-called idiopathic fragilitas ossium are cases of osteogenesis imperfecta. Case II. presented all the peculiarities which are characteristic of the cases usually spoken of as idiopathic fragilitas ossium, and would have been considered as such had I not elicited the information as to his condition at birth.

In very few of the reports of cases of fragilitas ossium is the condition of the skull mentioned. If they were seen early the skull was not examined, and when seen later, in childhood or as adults, the conditions at birth were not inquired into. However, the course of the disease, its undoubted congenital origin, and the scanty details of the early history are, I think, sufficient to enable us to definitely associate the condition with osteogenesis imperfecta. The following cases, one of which was observed by Griffiths<sup>1</sup> and the rest selected from some fifty-seven cases of so-called fragilitas ossium (nearly all of which are identical in their nature) collected by him from literature, are given here as examples of cases of osteogenesis imperfecta which figure in the literature as fragilitas ossium.

Griffiths' own case.—H. E., male. Nothing unusual noticed until the second day after birth, when it was found that the right femur was fractured. On examination under an anæsthetic it was found that the left femur was also fractured. Both fractures were treated and healed in three weeks. At the age of three months the right femur and right humerus were fractured during a medical examination. "As this was made with due caution, the bones were evidently very brittle. In March of the following year he again fractured the right femur, and in September the left femur. Two weeks after the dressings were removed from the left femur he refractured it.

"Besides these fractures there were times when he seemed to be having pains in various parts of the body, supposed to be rheumatic, but which were undoubtedly due to undiscovered fractures, since at least one of the thighs and one of the forearms, both of which united with angular deformity, were found afterward." On several occasions he has fractured ribs. It is estimated that he had in all seventeen or eighteen fractures. He certainly had twelve. The

<sup>1</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, vol. cxiii.

fractures were always attended by pain, but do not seem to have been preceded by it. Union has always been prompt.

"Examination. Plump and apparently well developed and healthy looking boy. The head is decidedly larger than normal. The frontal bones are enlarged, suggesting rachitis, and the back of the head is flattened, doubtless from continued pressure, caused by the enforced position. There was no evidence of possible rachitis connected with it. There is no beading of the ribs or enlarged epiphyses. The right arm has had angular deformity on the wrist, and the right thigh is similarly deformed at the upper third, with inversion of the foot." (There is no mention made of the condition of the cranial sutures at birth or thereafter, but from the description of the skull it is evident that osteogenesis was defective.)

Of the cases collected the histories are all very short, but many, if not all those with very numerous fractures, are cases of osteogenesis imperfecta. I extract only a few cases in which there can be no doubt of the diagnosis.

CASE XII.—Pritchard. A male child, apparently healthy, fractured both humerus and femur without history of accident two days after birth; on the next day broke the humerus through while being moved in bed, and in three weeks broke the other femur. All united promptly (the subsequent history is not given).

CASE XIX.—Blanchard. A woman, aged twenty-seven years, experienced her first fracture at the age of two months. Up to the age of nine years, when first reported, she had forty-one fractures. At twenty-seven years of age she was able to walk, and had about one hundred and six fractures. Her own weight was sufficient to break her legs, and she frequently had produced fractures while turning in bed. Not much inflammation and pain attended them, and no pain preceded. Union was remarkably tedious.

CASE XX.—A similar case reported by Blanchard.

CASE XXII.—Fleming. A man, aged twenty-four years, had his first fracture (thigh) when eighteen months old, and since has had in all fifty-three fractures. The simplest causes were sufficient. Union was remarkably prompt.

CASE XXVII.—Carson. A well-developed infant cried for five hours after a difficult birth. On the eleventh day a fracture of the thigh was discovered, and nine days after the other thigh was fractured. Two days later still the humerus broke, and at this time callus was discovered on the radius and ulna.

CASE XXX.—Schultz. A girl, aged thirteen years, was weak when born, but later grew well and strong. She had her first fracture of the femur at nine months. At one and a half years of age the same place broke again. Up to six years of age she had five more fractures without any trace of bending, and by her thirteenth year she had not less than thirty. All were produced by the slightest



causes. Pain was nearly absent in the fractures of the upper extremities, but present in those of the lower. Union took place in a shorter time than in normal bone. Great bending and twisting of the lower extremities finally developed.

The clinical histories of these cases show very plainly that they are identical with my two cases of osteogenesis imperfecta. In all of them the fragility of the bones was extreme; it was present at birth, and was not associated with any other abnormality. In Griffiths' case there is mentioned a peculiarity of the head, which is evidently the result of defective ossification. In the others this peculiarity is not mentioned, but the histories of these cases which I have looked up in the original are otherwise fragmentary, and it is probable that the skull in the young was not examined, and in the older individuals its condition at birth or soon thereafter was not the subject of inquiry. No doubt they were all similarly affected.

However, even if we leave this aside, it is evident that the principal features in all these cases, and in all others of a like character which have been carefully examined, are identical. They correspond so closely with the clinical features in the stillborn or premature infants with osteogenesis imperfecta, and they display so exactly the symptoms we would anticipate from a study of the pathological anatomy of this condition that there can be no doubt of the diagnosis.

Idiopathic fragilitas ossium and osteogenesis imperfecta are therefore only two names for the same condition, and in demonstrating this fact two points are definitely decided. One is that the foetus with osteogenesis imperfecta may survive fetal life and live to maturity; the other, that the condition until now known as fragilitas ossium, of which nothing was known, is the congenital or intra-uterine disease known as osteogenesis imperfecta.

In osteogenesis imperfecta the fractures nearly always begin to occur soon after birth, or they are already present, though perhaps unsuspected, when the child is born. The newborn infant is, as a rule, very weak, and for this reason is generally very carefully handled. In this event the infant may escape fractures for some time. As soon, however, as the general health improves and the child begins to move the extremities, or, as soon as he is less carefully handled, the extreme fragility of the bones becomes manifest.

The fractures of osteogenesis imperfecta are usually attended by less pain and less inflammation than those which occur in normal individuals. This, no doubt, is due to the fact that they are generally produced by insignificant violence, which causes less shock and less injury to the surrounding parts than would be the case were the violence great enough to fracture a normal bone. Aside from the minimal inflammatory reaction, the fractures are in no way peculiar. Union takes place rapidly, and is usually firm.

In some cases union takes place so rapidly that it is doubtful if a complete break has occurred. Both my cases show an angular bend forward in the lower end of the tibia which very closely resembles the deformity which often occurs in the same situation in rachitis. A large experience with rachitic children has taught me that this deformity is nearly always caused by infraction as a result of allowing the children to be on their feet while the bones are still soft and brittle. The great similarity between the deformity caused by infraction in rachitis and the deformity in the same situation in osteogenesis imperfecta, coupled with the extreme rapidity of the union which sometimes occurs in the latter disease, have led me to believe that this particular deformity and perhaps some other fractures of the latter disease are incomplete, that is, infractions.

However, though infraction may occur, the break is complete as a rule, and presents all the distinctive signs of fracture. The tendency to unite in deformity is no greater than in the normal individual. That these individuals present so many and such extreme deformations is not due to a specific tendency in this direction; it is due to the fact that the fractures occur so frequently that finally the individual or his guardian grows careless and does not give the treatment the required attention.

It is remarkable that in spite of the difficulties encountered nearly all those individuals who survive early childhood learn to walk. It is not improbable that after a time the affected individual becomes expert in the use of his limbs, and thus reduces the danger of fracture; but the fact that he learns to walk is not due to this cause alone. There can be no doubt that the fragility, though it never disappears entirely, diminishes somewhat with age. At any rate, sooner or later, during childhood, the cranial sutures, including the frontal, ossify, the fontanelles close, and these individuals certainly fracture the bones less frequently after puberty than before. Probably the active pathological process subsides at some time during intrauterine life or soon thereafter, and the fragility of the bones is simply the end result. But as neither the pathogenesis of the disease nor the anatomical conditions in adult life have been definitely ascertained, this cannot be positively affirmed. It is certain, however, that the intensity of the disease process is subject to some variations, for the patients present varying degrees of fragility. In some the process is very intense, and fractures occur as the result of the slightest exertion or precipitate movement; such individuals, of course, can never stand, and are compelled to lie in bed or in an invalid chair throughout their lives. Others, however, in whom the disease is of a mild character, finally get around very well, with only an occasional fracture to remind them of their abnormality.

The general health, after the first few months of infancy, is always

good. Nor do these individuals suffer from pain or other symptoms, except when a bone is fractured.

The differential diagnosis of osteogenesis imperfecta is comparatively easy. There is no other congenital disease in which there is such a uniform fragility of the entire skeleton. At times these infants are obese at birth, and if they are not carefully examined the condition may be mistaken for chondrodystrophia foetalis. However, only a little care in the examination will prevent this error. The two conditions, far from resembling each other, are directly opposite. In chondrodystrophia foetalis there is a decided prognathus or a flattening of the whole nasal region, the cranial sutures are normal or prematurely synostosed, the extremities are shortened, the bones are dense and hard, and aside from a slight bowing of the legs, are not deformed. In later life there is no danger of mistaking the two, for the adult chondrodystrophic individuals are dwarfs, with very short extremities and with absolutely no predisposition to fractures.

From rachitis osteogenesis imperfecta is readily differentiated. There is no beading of the rib, no enlarged epiphyses, no gastrointestinal or nervous disturbance, and the condition is always congenital.

It only remains to differentiate the fragility of osteogenesis imperfecta from that associated with other diseases. This is readily accomplished, for, with the exception of hereditary syphilis, none of the diseases in which multiple fractures occur is congenital. Osteomalacia is a disease which occurs after puberty, and, besides, presents other symptoms. Sarcoma and osteomyelitis are generally localized in a single bone, and have easily recognizable diagnostic signs. The same is true of the multiple fractures associated with nervous diseases and insanity. In rare instances it is possible that syphilitic epiphysitis in a newborn infant, with a separated epiphysis, which is mistaken for a fracture, might be confused with osteogenesis imperfecta. I have seen two cases of syphilitic epiphysitis in infants which were mistaken for fractures, and it is possible that in such an instance one might think of osteogenesis imperfecta. However, the other symptoms of congenital syphilis, which soon disappear, readily clear up the diagnosis.

In the cases of hereditary syphilis seen later in childhood which present no decided symptoms, but simply show signs of a vitiated constitution, the so-called dystrophia of syphilis, the differential diagnosis may not be so easy. Such children often have delicate bones, and are liable to fractures. These fractures do not, however, occur so frequently, nor are they produced by such insignificant violence as in osteogenesis imperfecta. Moreover, they do not occur during early infancy, but only begin to appear at or about puberty. If there is no history of syphilis the early childhood will be found to have been normal. The fractures are attended by

the usual inflammatory reaction and pain of fractures in normal individuals, and for these reasons they are treated properly, so that these persons do not present the numerous and grotesque deformities of those suffering from osteogenesis imperfecta. Besides, these individuals present the stigmata of heredosyphilitic degeneration.

If we adhere closely to the clinical symptoms—that is, fragility of the bones—which becomes evident at birth or soon thereafter, and is associated with defective ossification of the cranial vault, but with absolutely no other symptoms, I think the diagnosis of osteogenesis imperfecta will always be readily made. The majority of the cases of idiopathic fragilitas ossium so far reported present the symptoms of congenital fragility. That nothing of the condition of the skull during early life is mentioned is simply due to the fact that no one thought of making inquiries in regard thereto. Some of the cases, however, though classed by those who report them with idiopathic fragilitas ossium, do not belong in this category. These are the cases reported by Schuehardt,<sup>1</sup> Bruck,<sup>2</sup> and Anshutz.<sup>3</sup> In none of these was the fragility congenital. In Schuehardt's case the fragility came on at the twelfth year, and was caused by a general softening of the bones of the lower extremities. Bruck's case does not resemble Schuehardt's case at all, though this author places them in the same category. In Bruck's case the bones were brittle, but the fragility is said only to have appeared at the age of fourteen years; but the bones, though much deformed as the result of fracture, were not soft, as in Schuehardt's case. Besides the fragility of the bones, the joints throughout the body grew progressively more stiff, so that at the time of observation there was no joint in which there was free motion. Anshutz's case resembles Schuehardt's case somewhat, but is evidently not of the same character. The disease began acutely, with high temperature, great pain, and led to stiffening of the joints. It is evident that these cases are neither cases of idiopathic fragilitas ossium or osteogenesis imperfecta.

The cause and pathogenesis of osteogenesis imperfecta are as yet complete mysteries. In some instances the disease seems to have been hereditary. In neither of my cases was there a history of fragility of the bones in the family. Whether the general paralysis of the father in the one case or the drugs taken by the mother in the other had anything to do with the disease I am, of course, unable to say.

The treatment consists in simply placing the patient in a position to avoid fracture. If the disease is mild the application of the proper braces will be of benefit in so far as they protect the limbs.

<sup>1</sup> Die Krankheiten d. Knochen, Deutsche Chirurgie, Liep. 28.

<sup>2</sup> Deutsche med. Woch., 1897, No. 10.

<sup>3</sup> Mitt. aus f. Grenzgebieten d. Med. u. Chir., 1902, Bd. ix. S. 361.

The literature of osteogenesis imperfecta is given in full by Schmidt, "Pathologie d. Knochen," in Lubarsch's *Die Ergebnisse d. Allgemein Pathologie u. Pathologische Anatomie*; also in Ballentyne's book. That of fragilitas ossium may be found in Griffiths' paper in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, vol. cxiii.

## ERYTHEMA INFECTIOSUM.

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A FORM of eruption constituting in its symptom-complex a new exanthem was first recognized in Graz by Escherich. He had there an excellent opportunity to study r  theln during several epidemics, and was able to clearly differentiate another type of eruption which occurred about the same time. The clinical picture of r  theln as depicted in the literature has been clouded by the several different types of eruption and course of the disease which have been described. Those, however, who have had large experience with r  theln recognize it as having a distinct symptomatology which deviates only slightly from a certain definite type. The polymorphous forms heretofore described are most probably the result of wrong diagnoses. In no class of cases, perhaps, are so many mistakes made as in the skin eruptions of children. Escherich has rendered a distinct service by recognizing and classifying a separate exanthem which no doubt has long existed and has been masquerading under many names.

This disease was very accurately described by Tschamer<sup>1</sup> in 1886 under the name "Oerliche R  theln." The appearance over the cheeks, the eruption on the outer surface of the arms, its absence over the neck and trunk, and the duration of the eruption puzzled him exceedingly. He recognized he was dealing with a very different type of eruption from r  theln, but came to the conclusion that his cases were an abortive form of German measles. He had thirty cases which were similar in all essential points. A few years later an epidemic of the same eruption appeared in Graz, where it accompanied an outbreak of measles. Tschamer's cases were observed during an epidemic of r  theln. This epidemic was described by Gumpłowicz<sup>2</sup> in 1891 under the title "Casuistisches und Historische   ber R  theln," in which he agrees with Tschamer in its being an abortive type of r  theln. He showed that measles conferred no immunity over this disease, and *vice versa*.

Tobeitz<sup>3</sup> in 1896 read a paper before the International Medical Congress in Moscow entitled "Zur Polymorphie und Differential diagnose der Rubella," and confirmed the observations and con-

clusions of Tschamer. He reported a number of similar cases which showed "a distinct departure from the general course of rubella." He claimed this polymorphism was characteristic of rōtheln, and was produced by some change in the biology of the infecting organism effected by the season, surroundings, or some condition or idiosyncrasy of the individual. Escherich,<sup>4</sup> in the discussion following this paper, made the first claim that this form of eruption was not identical with rōtheln, but was a disease *sui generis*. He had a further chance to study this disease during two epidemics in Graz in 1897 and 1899. Schmid,<sup>5</sup> one of his assistants, gave a full description of the disease and its essential characteristics in 1899. He had observed one hundred and twenty-one cases.

Stricker,<sup>6</sup> of Giessen, also described in 1899 in a local medical journal an account of an epidemic of "Die neue Kinderseuche in der Umgebung vom Giessen, erythema infectiosum." He was the first to name the disease erythema infectiosum, and this term was accepted and adopted by Escherich. A full description of forty-five cases was given by one of Stricker's students in an inaugural dissertation.<sup>7</sup>

Tripler,<sup>8</sup> a pediatricist in Coblenz, described in 1901 an epidemic of seventy cases under the title "Erythema infectiosum febrile oder epidemischer Kinderrothlauf." An analysis of his cases shows them to be identical with erythema infectiosum, although some were accompanied with a slight fever. An epidemic occurring in Berlin in 1901 was described by Feilchenfeld<sup>9</sup> under the name "Erythema simplex marginatum," which occurred in the same families and in about the same locality.

Plachte,<sup>10</sup> a dermatologist, observed an epidemic of this same exanthem which he described in 1904 as "Megalerthema epidemicum die Grossflecken, ein neues Kinderexanthem." He does not think the term erythema infectiosum is descriptive of the disease, as it could be equally well applied to scarlet fever or measles.

Heimann<sup>11</sup> reported before a meeting of Niederrheinischer Kinderärzte at Cologne an epidemic of this disease which occurred in Solingen in 1903. He would term it erythema infectiosum morbilliforme on account of the similarity of the exanthem with measles.

Pospischill,<sup>12</sup> the attending physician to the contagious pavilions of the Wilhelmina Children's Hospital, made a preliminary report in 1904 on "Ein neues als selbständig akannta akute Exanthem." He gives a clear and unmistakable description of erythema infectiosum which he finds is not infrequent in Vienna. He differentiates it positively from measles, scarlet fever, and German measles. Cases have been sent to him with a diagnosis of measles or even scarlet fever.

The full report of these cases appeared in the *Wiener klinische Wochenschrift* for June 23, 1904, and in this article Pospischill states that the cases formerly described by him as scarlatinoid and

morbilloid were in reality erythema infectiosum, which he now recognizes as the diagnosis of his new exanthem.

The latest contribution on this subject is by Escherich,<sup>13</sup> who, in demonstrating two cases before the Gesellschaft für Aerzte, in Vienna, gives an historical review and the clinical features of this disease.

A careful perusal of the literature can leave no doubt that the form of eruption described independently by Tschamer, Escherich, Stricker, Plachte, Pospischill, and others is the same. These are all well-known men having a wide experience with the eruptive diseases of children. The priority of recognition as a separate disease entity belongs to Escherich.

A number of cases came to the out-patient department of the Annakinderspital in Vienna during the months of May and June, 1904, and through the kindness of Prof. Escherich I was enabled to study them. Dr. Henning, of the Allgemeines Krankenhaus, made the colored drawings from life, and also made moulages of the face and arm of one of the cases.

The description of erythema infectiosum has appeared only in the German literature, and this disease as such has not yet been recognized in America. The so-called "fourth disease," described by Dukes in 1900, differs in all essential respects, and will be considered later in discussing the differential diagnosis.

Erythema infectiosum may be defined as a feebly contagious disease occurring chiefly in children, with very slight subjective symptoms, and characterized by a maculopapular rose-red rash, more pronounced on the cheeks, legs, and outer surface of the arms.

The specific agent is unknown. The disease occurs in epidemics, and often follows an outbreak of measles or rötheln. It is found to spread through families, and a number of cases have been observed at the same time in schools and kindergartens. It is undoubtedly carried by contagion, but it is not so contagious as the other exanthemata. Cases have been taken in the wards of the hospital both in Vienna and in Graz, and no outbreak of measles or rötheln has resulted. An attack of any of the other exanthemata affords no immunity against erythema infectiosum.

The age most commonly affected is between four and twelve years. The youngest recorded case was in an infant, aged fourteen months, and several cases have been observed in young adults. It is essentially a disease of early childhood. Both sexes are equally affected. It occurs most frequently in the spring and summer months.

In cases where it was possible to make correct observations the period of incubation was from six to fourteen days. The disease may be ushered in by a slight feeling of malaise, weakness, and sore throat, but in the majority of cases the first symptom noticed is the eruption. This is the most important and often only symptom.



Erythema Infectiosum.







*Erythema  
infectiosum*

Erythema Infectiosum.



It appears invariably on the external skin, and no constant changes on the mucous membranes have been observed. A diagnostic feature of the disease is the character of the rash on the face, where it first makes its appearance. The cheeks are chiefly affected, and present a symmetrical rose-red efflorescence. The skin is hot to the touch, and is swollen, but it is not at all sensitive and does not itch. The color disappears on pressure, but quickly reappears. The whole appearance is suggestive of erysipelas. The eruption is confluent over the cheeks, and the edges are well defined, slightly raised, and distinct from the normal skin, but it may gradually fade on to normal skin. This area of confluent eruption is rather sharply limited in front by the nasolabial folds, and above by the temples. Laterally it extends to the angles of the jaws. The skin around the mouth appears pale in contrast to the livid hue of the cheeks. Discrete spots, varying in size from a pea to a hazelnut, are often seen on the forehead and chin. The rash fades from the face after four or five days. On about the second day the eruption makes its appearance on the body, where it is most marked on the outer surface of the arms and legs. The trunk is involved to a much less degree, and may be almost free, but in no case was the rash so intensive as on the face and extremities. The eruption spreads toward the periphery, and the hands and feet are the last portions of the body to be affected. On the extremities the exanthem is typical and characteristic. It is morbilliform in appearance, and not so deeply rose-red as on the face. The contour of the eruption presents frequently almost geographical outlines, and in many cases the appearance is suggestive of lacework, especially as it begins to fade at the end of the disease. On the inner or flexor surface of the arms the eruption is not nearly so intense. It is apt to become confluent around the outer surface of the elbow. On the legs the eruption is similar to that on the arms, and it is always especially well marked over the buttocks. The trunk remains comparatively free from eruption, although a number of discrete spots, sometimes crescentic in form, can be seen sparsely scattered over the chest and back. The rash is more macular than papular, and shows only a slight elevation, except on the face, where it is always raised. An evanescence is often observed which is perhaps peculiar to this disease. The rash will apparently disappear when some slight irritation to the skin, such as friction, exposure to cold, etc., will bring it out again in full bloom. The eruption is not followed by desquamation. It lasts from six to ten days, and does not leave any stains or markings such as are sometimes seen after measles. No hemorrhage results on pinching the skin as occurs in measles and scarlet fever. The lymphatic glands are not enlarged as a result or accompaniment of this disease.

The subjective symptoms are conspicuous by their absence. The tongue may be slightly coated, but it never presents the straw-

berry appearance and desquamation of scarlet fever. The conjunctivæ are not congested, and there is no coryza or cough. The urine is normal. The prognosis is absolutely favorable, and in none of the epidemics have any complications or sequelæ been observed. The disease is interesting chiefly from a medical point of view, and especially in reference to diagnosis. The care and welfare of the patient and the protection of other members of the family and of the community depend to a great degree on an early and accurate diagnosis of the acute exanthemata of children. The expense involved in the maintenance of quarantine, the services of a trained nurse, etc., is considerable, and a great injustice is wrought when a wrong diagnosis is made and a child unnecessarily placed in seclusion.

The disease most likely to be mistaken for erythema infectiosum is rōtheln. This disease, curiously enough, was first recognized by the Germans toward the end of the eighteenth century, and hence is derived the name German measles. In this disease prodromal symptoms are not uncommon, and the rash spreads rapidly over the entire body, and especially on the chest and back. The rash appears first as small, discrete spots, somewhat larger than the punctate spots of scarlet fever, and smaller than the papular rash of measles. The favorite seats of the rash on the face are the region around the mouth, back of the ears, and on the forehead. The color of the eruption is pale pink. The lymph nodes, and especially those of the post-cervical group, are invariably enlarged, and while there may be only a few constitutional symptoms yet a temperature of 103° is not uncommon. The appearance, location, and spread of the rash in erythema infectiosum is entirely different. The lymph nodes are not enlarged, and in only a small percentage of the reported cases was any fever detected. During all three of the epidemics in Graz erythema infectiosum was often seen in children known to have had rōtheln or measles. As it accompanied or followed outbreaks of these diseases, this point was easy to establish. As it not infrequently is associated with these diseases, the importance of the differential diagnosis is all the greater.

Measles can be excluded by the absence of all involvement of the mucous membranes, of all constitutional symptoms, and the uniform absence of the Koplik spots. The appearance of the rash on the arms and legs is strikingly similar to measles, and may cause a momentary confusion, but a further examination will clear up the diagnosis. The question of its being a second eruption of measles with atypical symptoms has been raised. This is not tenable, from the fact that erythema infectiosum very often occurs in children who have never had an attack of measles. It is more probable that the so-called recurrent attacks of measles are in reality cases of erythema infectiosum.

Scarlet fever should present no difficulties, although this diagnosis has more than once been made in cases of erythema infectiosum.

The throat symptoms, color appearance, and location of the rash, the constitutional symptoms, etc., have nothing in common with erythema infectiosum.

Erythema exudatum multiforme, which was first described by Hebra,<sup>13</sup> presents more similarity in name than in clinical features. Here the back of the hands and feet are first affected, while in erythema infectiosum the face is the first and most characteristic seat of the eruption. In the Hebra type the rash is first macular, then papular, and later vesicular, and the disease lasts for three or four weeks, and is generally accompanied with severe constitutional symptoms. It is never contagious, and can often affect the same person.

Pityriasis rosea presents some similarities in the skin lesion, but it seldom affects the face, is never contagious, and runs a chronic course of from eight to ten weeks.

Drug rashes, toxic and dyspeptic erythemas, can all be differentiated by the history. At first sight these rashes, especially the serum and toxic erythemas, are very similar to the rash of erythema infectiosum. The specific cause, the duration, location, and course of the eruption should remove any possibility of confusion. The same can be said in regard to urticaria, where the further absence of itching and of the characteristic wheal formation makes the diagnosis clear.

Very little has been heard of the fourth disease in the past two years, and the medical profession seems to have accepted Ker's verdict of "not proven." Any description of a new exanthem will at once recall the article of Clement Dukes,<sup>14</sup> which appeared in 1900, entitled "On the Confusion of Two Different Diseases under the Name of Rubella (Rose-rash)." The rash which is the characteristic feature of both diseases is very dissimilar. In the fourth disease the body is covered in a few hours with an extensive rash. The color is bright red, and from the character of the rash alone "it is impossible to distinguish it from scarlet fever." The face often remains free from any signs of the eruption. Profuse desquamation follows in a number of the cases. Without entering into a further discussion of this disease, it will be plainly seen that the essential characteristics of each disease are different. Ker,<sup>15</sup> of the Edinburgh City Hospital for Infectious Diseases, in discussing the question, "Is there a fourth disease?" said that he had long been prepared to hear that there was a new disease hitherto confounded with röteln, but he could not be convinced that the fourth disease of Dukes met all the requirements. The disease I have endeavored to describe lies nearer to German measles than to the other types of recognized exanthemata, and may be the disease heralded by Dr. Ker.

The object of this paper is to call the attention of the American medical profession to a disease which has been described inde-

pendently by several well-known pediatricists, and which has clinical features distinct enough to justify its classification with the acute exanthemata.

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### A CASE OF AMAUROTIC FAMILY IDIOCY.\*

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THE patient, Abe G., aged one year, was brought to the Children's Dispensary at the Polyclinic Hospital by Dr. Leo H. Bernd, September 15, 1902.

*Family History.* The mother is healthy, and had four sturdy children by a former husband. She has never miscarried. The father, too, has been twice married, his first wife dying in childbirth during her first confinement. The baby also perished. The patient is the first-born of the present union. There is no history of insanity, imbecility, tuberculosis, or syphilis in the family of either parent. The father has been out of work a great deal, and poverty has been the consequence. At times he has been unable to procure sufficient food for the family.

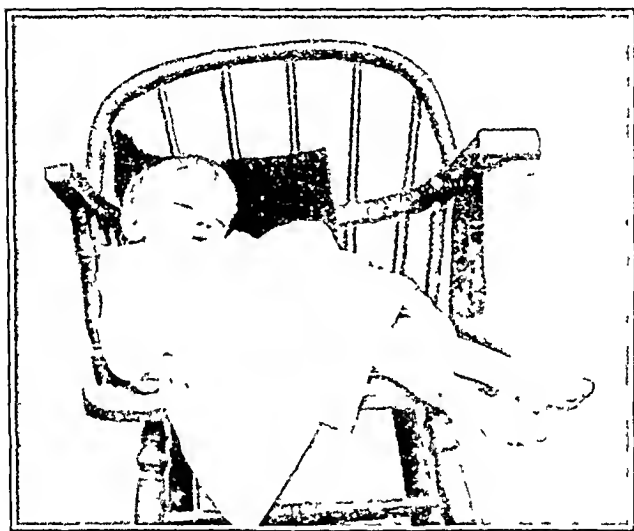
*Personal History.* The patient was born at full term, and was considered a normal baby. He was breast-fed during the first year. About four months ago he had considerable fever for a few days. Recently an eruption appeared over his body, but it disappeared very rapidly. Several months ago he fell from a chair, since which time, the mother states, he has been unable to properly support his head. His bowels have always been constipated, and he takes cold easily.

*Status Præsens.* He presents a square rachitic head, with a widely open, though not depressed, fontanelle. There are no teeth,

\* Read before the Philadelphia Pediatric Society, June 7, 1903.

but four incisors appear ready to erupt. He is very fat and flabby, has a marked lumbodorsal curve, beading of the ribs, and an enlarged liver and spleen. He does not support his head, sit upright, nor stand.

After this initial examination, he was seen at our clinic on September 24, October 9 and 29, November 13, December 31, 1902, and January 7 and 28, 1903. At these times he was treated for rachitis, for constipation, and for repeated attacks of bronchitis. The first disease was much improved, his dentition progressing, his nutrition being bettered, and his motor development advancing to a point where he could stand with slight assistance. This last accomplishment he manifestly enjoyed. He did not learn to speak, though he understood much that his mother said to him. At the last visit mentioned he was given thyroid extract.



A. G., aged seventeen months.

*March 4, 1903.* The mother reported that the baby did not take any notice of his surroundings, and she thought that he was blind. She also stated that he did not use his arms for grasping, etc.

*April 8th.* The patient was seen after my clinic hour, and after a somewhat careful examination a tentative diagnosis of amaurotic family idioey was made. Dr. Bernd referred him to Dr. Mary Buchanan for confirmation of this opinion. We endeavored to take him into the Polyelinic wards, but as there was no vacant bed there he was referred to Dr. Griffith, at the University Hospital.

*May 17th.* The child has been in the University Hospital since the last visit.

He shows craniotabes and a depressed fontanelle. Chewing movements are repeatedly executed. His canine teeth have erupted, but not the incisors, so that dentition has progressed in a most



aberrant manner. The teeth are dark, and the enamel covers them but imperfectly. The tongue is coated. The ribs are soft and there is marked beading present. Palpation and percussion of the chest reveal nothing of importance, but posteriorly sonorous rales are heard over the larger bronchi. The second pulmonic appears to be the loudest of the cardiac sounds, and is much sharper than the aortic second sound.

The lower hepatic border extends almost to the level of the umbilicus in the right mammary line. The spleen is palpable slightly below the costal margin. There is a small capillary naevus on the front of the right thigh. The lymph nodes are enlarged in the posterior cervical chain of the left side, and one enlarged gland is present in the right chain. The axillaries are not palpable, but the supraclavicular nodes are felt. The inguinal glands are slightly enlarged.

*Nervous Phenomena.* The head rolls about when the child is moved, indicating paresis of the neck muscles. The limbs are spastic. The forearms are extended upon the arms and fully pronated. The appearance of the claw-hand is well exhibited, and there are vermicular movements of the fingers resembling but much slower than athetoid movements. The thighs and legs are fully extended, as are the feet. The great toes are extended and the other toes flexed as in the Babinski-phenomenon. When the child is disturbed, the left side of the face, the left arm and leg are moved more freely than the corresponding parts upon the right side. The tongue apparently moves normally. The biceps, flexor and extensor jerks are much increased. The extreme spasticity of the lower extremities interferes with the study of the knee-jerk. Ankle clonus is present, but is not marked.

The plantar reflex is excessive, the whole leg upon the side tested being thrown into spasm. The Babinski reflex is also present. The electrical reactions were not studied.

*Sensory.* The left pupil is widely dilated and does not respond to light; whilst the right is but moderately dilated, and responds rather well. The baby is unquestionably totally blind. A restless lateral to-and-fro movement of the eyes is present at intervals, but is not rapid enough to be styled nystagmus. Dr. Buchanan reports that the eye-grounds exhibit the picture characteristic of Sachs' amaurotic family idiocy. There is hyperacusis, the patient starting markedly when one's voice is elevated. Tactile sense and deep pressure sense are present, but the response to stimulation is very slow. Taste is present, for the mother states that the baby shows a preference for certain foods, notably for orange-juice.

Mentality is at a very low ebb. The infant is exceedingly somnolent and is hard to disturb except by sounds, and when so disturbed the cry is at first weak and fretful. After a time it may become quite strong. As recorded, there has been no speech.

The respiratory rate is 30 to the minute, and the pulse is 136 (after crying). Both are regular. The temperature is normal, though at one previous visit it was  $95.6^{\circ}$  per rectum.

*May 27th.* Prior to three days ago, the mother declared that the baby was better, but at that time he contracted another cough. His temperature is normal. The examination of his chest again reveals very little, though the sonorous rales are more marked than at the last visit, and are more numerous over the right bronchus posteriorly than over the left. His cough plainly causes him pain. The adenopathy is unquestionably becoming more conspicuous. The head is retracted and the muscles of the back of the neck manifest considerable resistance to an effort to bring it forward. The back is also stiff. The epigastric, abdominal, and cremasteric reflexes are not only accentuated, but the responses follow the stimuli very quickly.

The history detailed and the interesting physical findings lead one to the inevitable conclusion that the patient has amaurotic family idiocy.

Sachs has summed up the principal symptoms of this curious affection as follows:

1. Mental impairment appearing during the first months of life, and leading to absolute idiocy.

2. A paresis or paralysis of the greater part of the body, and this paralysis may be either flaccid or spastic.

3. The reflexes may be normal, deficient, or increased.

4. A diminution of vision terminating in absolute blindness, changes in the region of the macula lutea, and later optic nerve atrophy.

5. Marasmus, and a fatal termination, as a rule, about the age of two years.

6. The occurrence of the disease in several members of the same family.

The first four conditions are certainly fulfilled in the present case, though marked mental impairment did not take place, or at least was not sufficient to attract the attention of the parents, until a later period. The fatal result would probably have occurred somewhere in the last fortnight, had it not been for the great devotion of Dr. Bernd, who has actually supplied this family with food.

With regard to the occurrence of the disease in other members of the family it must be borne in mind that we are studying the primogeniture of the present union, and that the only child of the father by his first wife died. The mother is pregnant at the present time, and we shall possibly be able to learn whether the family tendency is existent. This last characteristic is not an absolute essential, however, for though there were four subjects of this disease in the family recorded by Tay, and though the sister of Sachs' first recorded case developed the same disease, there are unques-

tioned examples of single occurrences in families; for instance, Clairborne's case.

One may add that the present patient exhibits additional phenomena to those recorded above—viz., the somnolence and the curious vermicular movements of the fingers and hands, of which Clairborne speaks.

While the diagnosis of the disease under discussion is easy in the present instance, there are certain clinical features that also suggest the possibility of both chronic meningitis and brain tumor. The marked adenopathy lends some support to one or other of these views, while at the same time it would furnish a possible etiological explanation of either morbid process. The case reported by the last-named author, together with the autopsy finds of Chamberlain and Holt, showed that a tyroma of the corpora quadrigemina might exist in a well-marked amaurotic idiot. So that the diagnosis of brain tumor at least is not incompatible with that of amaurotic family idiocy. The writer wishes it distinctly understood that he does not make a diagnosis of meningitis or brain tumor, but that both have been suggested by the study of this patient and retained as mental reservations.\*

When one has referred to the original report of Tay,<sup>1</sup> in 1881, who gave a classical description of the eye-grounds in this curious disease; to the paper of Sachs<sup>2</sup> (1887), who described and named the disease under discussion, wholly unconscious of the reports of Tay and other ophthalmologists; to the discovery of Kingdon,<sup>3</sup> who called attention to the fact that Tay and Sachs had from different standpoints reported the same disorder; to the interesting observation of Carter<sup>4</sup> (1894), who showed that all of the reported patients were Jews, one has traced, in brief, the development of our clinical knowledge regarding amaurotic family idiocy. Add to this the pathological work of Sachs, Russell and Kingdon, Peterson, Hirsch, and the finds of Holt in Clairborne's<sup>5</sup> case, and one has completed the story.

But it was not until Sachs<sup>6</sup> contributed his paper in 1896 that interest in this disease may be said to have become widespread. In that year the author named was able to collect but 19 cases from the literature, while in 1898<sup>7</sup> he collected first 27 and later 28.

It is interesting to search such classical works as Gowers, Hirt, Keating, Holt (first edition), and Rotch (first edition) and find no mention at all of Tay's disease or of amaurotic family idiocy. Even at a later day the subject has not received the attention from authorities that its importance seems to merit; thus the *Twentieth Century Practice* does not deal with it at all; and in a recent work upon pediatrics I have been able to find no reference to it.

Since 1898 cases have been reported by Jacobi (3 cases), Patrick,

\* The second baby presents no evidence of the disease at one year of age.

Kuh, Welt, Kakels, Pinekard, Clairborne (his own and one cited to him by Pooley), Cotton, etc. Indeed, in 1901 Falkenheim<sup>8</sup> succeeded in collecting 64 cases. His paper is a masterful contribution to the literature of the subject. Sachs reported still another case in 1903, together with an interesting and careful post-mortem study. He thinks that it is no longer necessary to tabulate cases. That they are of much more common occurrence than these figures signify no one who has studied the subject can fail to perceive. Thus, Clairborne states that he has seen 5 cases, though he does not state whether they were all his own; and also adds that at the Mt. Sinai Hospital 6 cases had been observed. One of these was probably Heimann's reported case. Morse, of Boston, in discussing Cotton's paper, remarked that he had seen 3 cases, one of them in an American. Last year Drs. Hamill, Spiller, and Posey told me of a case that they had seen in Philadelphia.

In studying what is known of the etiology of this affection, one enters upon mooted soil. That most of the patients afflicted are born of Semitic parents, all contributors to the subject are agreed; but Sachs prophesied in 1898 that it would be found to exist among other people, and two reported and one mentioned case have served to fulfil his prediction. More cases have been observed in girls than in boys; thus of Sachs' 28 collected cases, 14 patients were girls, 9 were boys, and in 5 the sex was not mentioned. Again, it is essentially a disease of early infancy, the victims being attacked, as a rule, between the second and the tenth months of life.

With regard to pathological findings and the interpretation thereof, however, we meet with two contrary views—viz., that of Sachs and that of Kingdon and Russell.

The former, strong in his convictions, and ably supported by Peterson, contends that the disease represents an arrest of development of nerve cells, and possibly of the white fibres, and allies it with Friedreich's ataxia, hereditary cerebellar ataxia (type Nonne-Marie), hereditary spastic paralysis and the like. Kingdon, strengthened by the work of Wm. Hirsch, who made a splendid pathological investigation, and endorsed by Jacobi, believes the disease process to be a degenerative one. Hirsch's work would seem to have proved this latter view, and he alluded to mothers' milk as a possible carrier of infection. Sachs, replying to Hirsch, stated that several of these patients had been fed artificially, and also maintained that cells whose development had been arrested would of necessity degenerate. In his last contribution Sachs supports his original contention most ably, and appears to have the better of the argument.

While studying this subject, the writer was struck by a passage in Hektoen and Riesman's *Pathology*: "The anatomical basis of chronic degenerative chorea (Huntingdon's chorea) may be considered as degenerative disease of the cerebral cortex. The morbid

anatomy of this disease is now fairly well established. There may be some hesitancy in admitting the disease to the category of encephalitis, as in reality the disease is a teratological defect of the ganglion cells, the changes in the mesoblastic cells being secondary and dependent. The ganglion cells in individuals who develop Huntingdon's chorea are endowed with a specific energy or vitality to enable them to exist only a certain length of time, although it should be understood that they have the full potentiality of development, and the possessor may have enjoyed the fullest complement of mental development before the period of decay is at hand."\* In amaurotic family idiocy the development until then normal ceases at a very early age; but there are some clinical and more pathological resemblances between this disease and Huntingdon's chorea. It might be said, hypothetically, that the "specific energy" of the cell in amaurotic family idiocy permits it to exist for a *very* short period of time. Gowers suggests the term "abiotrophy," to indicate such predestined short life of cells. (See Sachs' last paper.)

In both of these pathological processes it may be to the sperm cell or the ovum that we must look, and possibly to the chromosomes of these cells.

It has occurred to the writer that possibly a nutritive or metabolic factor or factors might account for both the arrest of development and the degeneration occurring in this disease.

Weissmann, in speaking of the continuity and practical immutability of germ plasm itself, admits that it may be slightly modified by nutritive causes. A careful study of the normal chemical and histological elements of the blood, and of its possible bacteriology, and also an extended study of the secretions, might settle the point as to whether or not an infectious agent is operative here; or such investigations might reveal something of importance in support of a metabolic hypothesis. It is regretted that opportunities for such studies were not afforded in the present case.

The writer begs to submit the following facts: The disease is most common among the progeny of a hardworking, self-denying race, and a race in which the neuropathic element is a very pronounced one. Another disease in which there is disordered metabolism is common among Semitic peoples—viz., diabetes mellitus, and the affection is frequently observed in several generations of a family. The developing impregnated ovum is wonderfully protected against both infectious and nutritive causes of a blighting

\* Among different races one finds that the period of active development of the cerebral cell varies; thus, Charles Darwin speaks of the way in which the full-blooded African and the Caucasian youth may be educated side by side, but in one intellectual advancement ceases a number of years before the other has attained his mental maturity. In studying the lives of the truly great, one is struck by the intellectual achievements of many of these men at an age when their less favored brethren have passed into the period of

"The lean and slippered pantaloons,  
Sans teeth, sans eyes, sans taste, sans everything."

character, but the growing embryo and foetus can be affected by the environmental factor of innutrition or malnutrition (the parents of the present patient have actually been pinched by starvation). Again the nursing child may be suckled with a milk insufficient in important constituents to meet its growing demands. Lastly, these patients are always far below par, nutritively, are subject to repeated attacks of bronchitis, exhibit weak digestive organs, and finally perish of marasmus.

As a control statement it is necessary to admit, however, that, taken seriatim, most of these theoretical considerations may be advanced in favor of an infectious cause. The repeated attacks of bronchitis probably occur because of the little one's poor resisting powers. The father of Clairborne's patient had advanced pulmonary tuberculosis, and the tuberculous lesions in the baby probably represented true complications and not essential parts of the disease, amaurotic family idiocy.

The questions of pathology, symptomatology, differential diagnosis, and prognosis, the writer will not treat here, because they are all ably dealt with elsewhere.

With respect to treatment, Sachs states that it might be advisable to prevent conception in these families had not healthy children been born to the parents of several amaurotic idiots. The writer would suggest a most strict hygiene of the mouth and nasopharynx in subjects of this disease, bearing in mind the suggestive work of Spiegelberg in the study of the bacteriology of the pneumonic complications of gastrointestinal diseases. He believes that the frequent infections of the lower air-passages occur from these situations.

If, in the future, a nutritive or metabolic cause be found responsible for or operative in this disease, some animal therapy may serve eventually to successfully combat it.

*Subsequent History.* During the summer (1903) the patient's nutritive condition perceptibly improved, particularly during the weeks spent at the Children's Seashore House at Atlantic City. With the onset of cooler weather, however, he failed to do so well, and again suffered repeated attacks of bronchitis. His nervous condition remained practically unchanged.

On January 3, 1904, I referred him to St. Christopher's Hospital, and he was admitted the same day to Dr. Tully's service at that institution. With Dr. Tully's kind permission, Dr. Philip Norris, interne at the hospital, courteously sent me a copy of his subsequent history and chart. Appended is a brief abstract of the notes furnished by Dr. Norris:

During the early days of his stay in the hospital the patient's state of nutrition underwent little change, but from January 16th, when he weighed 15 pounds, he progressively lost flesh, and on

February 22d, the day before his death, he weighed but 12 pounds. His bowels were constipated at first, but became quite loose in February. Occasionally they were green and contained mucus, and at times they were offensive. Tympanites was marked upon several occasions.

His temperature was irregularly remittent, strongly suggesting the possibility of tuberculous disease. The lowest recorded temperature was 95°, the highest 103°. The respiration rate was rather low at first, and apparently not always commensurate with the temperature. For two days (February 12th and 13th) his breathing was of the Cheyne-Stokes type. With the onset of the catarrhal pneumonia, the respirations became accelerated. On February 12th the chest was found "full of large mucous rales," but no consolidation was demonstrable until five days later, when dulness upon percussion was found at both bases.

The pulse was weak throughout his stay at St. Christopher's Hospital, and on several occasions it was not perceptible at the wrist. Irregularity of the pulse was also present at intervals. Coldness and cyanosis of the extremities were frequently observed.

The nervous phenomena, as described in Dr. Norris' notes, differed but little from our own findings, as recorded. The same variability in symptoms and signs were observed, however, that one sees so usually in meningitis. Thus upon one day, general anæsthesia was found, the soles of the feet alone appearing sensitive to touch. On the very next day, however, hyperæsthesia existed. Some studies of the electrical reactions were made. On February 17th, strong galvanic and faradic currents were required to elicit any muscular response, "especially in the muscles of the neck." On February 18th, much weaker currents were required to produce contractions, but the reactions of degeneration were present in the neck muscles.

Dr. Krause, ophthalmologist to the hospital, made the following notes (January 18, 1904): "Fibrillary tremor, particularly in the upper lids. Vertical nystagmus. Eyes in normal position. The pupils dilate fully and equally under atropine. O. S. media clear. Disc oval, 90°, extremely pale and white. Trophic excavation. The arteries and veins are much contracted."

On February 21st he had a slight general tetanic convulsion. Early in the morning, February 23d, a number of tonic and clonic convulsions were observed by the nurse. They were largely confined to the extremities, and the average duration was thirty seconds. At 4 A.M. he had a more protracted convulsive seizure, lasting about two minutes, and two hours later he died quietly.

A necropsy was held fifteen hours later, but four hours after death the vitreous humor was drawn off with a hypodermic syringe, and each posterior chamber was filled with a 10 per cent. solution

of formalin. (The eyes were splendidly hardened as a result of this procedure, and the retinae were well preserved).

The autopsy revealed an extensive catarrhal pneumonia, involving both bases posteriorly; a general adenopathy, and a number (six) of agonal intussuscepta of the ileum. The veins of the pia were much distended, and the brain itself was exceedingly heavy and œdematous, rendering its removal difficult. The brain and cord were removed with little injury, however, and were sent to Dr. Spiller. Dr. Buchanan removed the eyeballs. Sections were cut from thymus, thyroid, lymph nodes, and adrenals, and were preserved for the pathologist; but I have secured no report upon the same. There was no macroscopic evidence of tuberculous infection.

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## OCULAR MANIFESTATIONS IN AMAUROTIC FAMILY IDIOCY.

BY MARY BUCHANAN, M.D.,  
OF PHILADELPHIA.

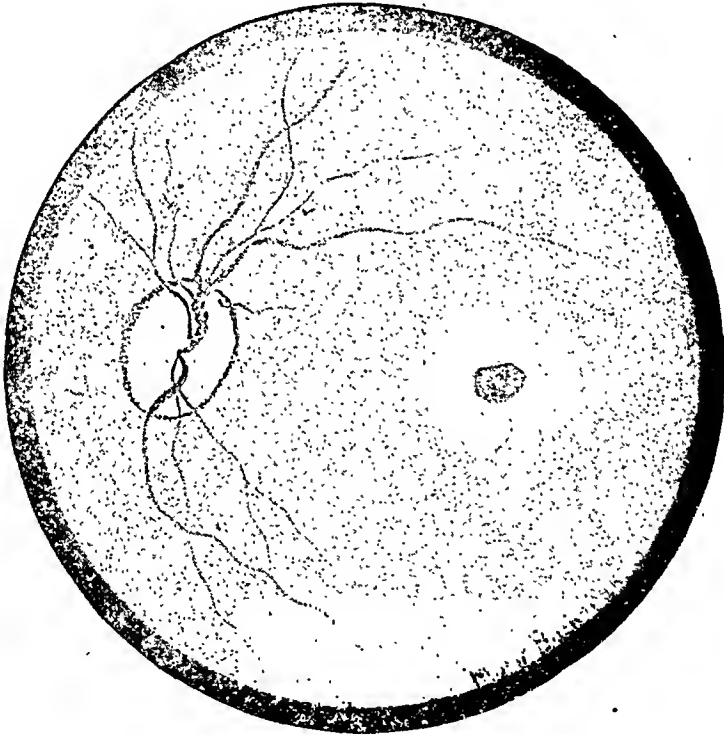
A. G., the patient, was sent to me by Dr. McKee on April 22, 1903, at which time he was so depressed that a satisfactory fundus examination could not be made. The pupils were about 4 mm., non-responsive to diffuse daylight, but the eyes were constantly rolled up and in, the pupils being contracted with convergence, making a view of the macular region impossible without a mydriatic. Another visit was requested, but instead the child was taken to the University Hospital, where the diagnosis was confirmed by Dr. de Schweinitz.

On May 18th following, the patient was again examined by the writer, after leaving the University Hospital. His physical condition showed considerable improvement. At this time the pupils were unequal, the right 4 mm., responding to condensed light; the left 5 mm., non-responsive. The media were clear, showing a scleral ring out, and a very marked pigment ring beyond. The



disks were atrophic and bluish-white in color. The vessels were very much reduced in size, especially the arteries, which, in the left eye, were so small that it was very difficult to trace them over the red eye-ground. The retinal pigment was absent in many places.

The macular region in each eye showed the pathognomonic condition. The fovea showed as a dark-red oval with sharply defined edges, the color corresponding to that of the veins. At its centre a tiny yellow reflex was seen. Surrounding the fovea was a large, greenish-white, oval patch, very dense at the fovea, and gradually fading away toward the periphery. Several minute retinal vessels were traced over the white area. In both the fovea and the surrounding oval the long axis was horizontal, the latter measuring about one and one-half disks' diameters.



A. G. Left eye-ground at eighteen months.

A few words to those unfamiliar with ophthalmoscopic examinations may not be amiss. The special point of interest lies in the macula, which, in a normal eye, is red, like the rest of the fundus, except that it is a trifle darker and has no vessels visible upon it, while in amaurotic idiocy the macula is always occupied by the oval white patch surrounding the fovea, as previously described.

The optic disks, normally, are transparent, with numerous arterioles passing through the nerve, which, although not differentiated by the examining eye, give a healthy, yellowish-red hue. Here the

nerve heads have a hard, white, opaque look. All the tiny vessels have disappeared.

The vessels in the normal eye are round and full, the arteries being about two-thirds the size of the veins, showing the light streak. Here the arteries are very small, in fact scarcely traceable over the red fundus, and the light streak is absent.

The pigment ring which surrounds the disk is normally softened in outline by the nerve fibres passing over it, but here it stands out with startling distinctness, marking the degeneration of the fibres.

All descriptions of the macular conditions in this disease agree fairly well, variations in the tint of the white area being due to the kind and amount of light used in the examination. It is often described as a bluish-white or dead white. The disks have been reported healthy in some cases and the vessels normal in size, but the majority have had optic atrophy, at least late in the course of the disease.

Strabismus and nystagmus have been reported present in several cases, but they were incidental.

The movements of the eyes are free and constant. The pupils generally respond to light somewhat, if only sluggishly. Dr. Clairborne's case showed external squint and ptosis of one eye, and is noteworthy from the facts that the patient was not of Hebrew extraction, had a distinct tuberculous family history, and the autopsy revealed a tuberculous tumor of the corpora quadrigemina, and tubercles through the lungs, spleen, and bronchial glands.

Dr. Cotton's case resembled ours in the inequality of the pupils and in the spasms which the slightest noise or jar brings on, in which the arms and legs are rotated internally and adducted, and the whole body slightly involved. During one of these spasms the writer noticed that the pupils, which had been about 2 mm. in diameter, almost equal, and active to light, were suddenly dilated to 5 and 6 mm. in the right and left respectively, non-responsive to strong illumination, remaining so for half an hour, although the spasm lasted only a moment.

Although amaurotic family idiocy was first discovered and described by Mr. Waren Tay, an ophthalmologist, in 1881, no explanation as to etiology and pathology was vouchsafed. Very few eyes have been obtained for microscopic examination. Mr. Treacher Collins made slides from the eyes in Mr. Kingdon's case, and reported that the choroid was healthy, but that the retina had been thrown up into a fold around the macula, rendering the retinal examination unsatisfactory. It showed a spacing out of the outer reticular layer, which he regarded as indicative of œdema. These folds always produce such spaces, however, even in healthy eyes.

Dr. B. Sachs was the first to realize the general nature of the disease, and after a thorough microscopic examination of the

cortex he decided it was an arrest of development. It remained for Dr. Hirsch to make a complete examination of the cortex, the spinal cord, and of the basal ganglia with the improved methods of staining and hardening, to determine that it was really a degenerative process.

Dr. Ward Holden, who made a pathological report on the eyes of Dr. Hirsch's patient, was the first to show the relationship between the fundus condition and the general nervous affection. By securing the eyes four hours after death, before post-mortem changes had begun, and by hardening one eye in 10 per cent. formol, he obtained a specimen in which the retina stayed in position at the macula. To avoid error he also prepared the eyes of an infant dead of the same disease (pneumonia) in exactly the same way.

In the normal eye the ganglion cells vary from 10 to 30 microns in diameter. In the periphery, where the cells are scattered, large cells abound; but in the macular regions, where the ganglion layer is several cells deep, the cells are small, irregularly pear-shaped, and packed closely together.

Sections of the diseased eye in this case showed the average size of the ganglion cell to be increased, and the average shape to be altered toward the globular. In Nissl preparations of the formol eye, with a one-eighteenth immersion, the cell membrane and cell reticulum could be made out, but no Nissl granules were present, and the cell body had the appearance of having had its liquid contents withdrawn. No actual œdema of the retina was found. The other layers were apparently normal. The ciliary nerves were normal and the ganglion cells of the ciliary body did not give these reactions. The optic nerve showed an absence of myelin in many fibres, and the neuroglia tissue was increased—simple degeneration.

Comparisons with the preparations of the brains of the patients of Drs. Sachs and Hirsch show the staining reactions in the cerebral and retinal cells in each case were identical.

The changes in the fundus are explained by the changes in the ganglion cells. In the fovea the ganglion cells are absent. At the margins of the fovea the ganglion layer is six to ten cells deep. One disk's diameter from the fovea horizontally it is three to four cells deep; two disks' diameter, two or three cells deep, till at the periphery it is a scattered layer of single cells. Hence we have the red centre destitute of the cells with the choroid showing through, next the dense white, corresponding to the deepest portion of the layer, fading away gradually as the cells become fewer. In the vertical meridian the ganglion-cell layer thins out more rapidly than in the horizontal.

The optic nerve atrophy Dr. Holden regards as both an ascending and a descending degeneration; a breaking down of the neuraxons of the affected retinal ganglion cells and of the affected ganglion cells of the basal ganglia.

The ocular neurons have undergone a primary alteration like the cerebral neurons, both being embryologically related, developed from the same medullary tube of the involuted ectoderm.

The cerebral degenerative progress can be marked by examining the eyes. These are normal at birth; at three months there is a haziness in the macular region, and the picture is complete generally by the sixth month.

The pathology is very satisfactory, but the etiology is still awaiting the genius of a Sachs, a Hirsch, or a Ward Holden.

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## HISTOLOGICAL EXAMINATION OF THE EYES IN A CASE OF AMAUROTIC FAMILY IDIOCY.<sup>1</sup>

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AND

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(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

THE eyes upon which we desire to report are from a patient presented by Dr. James H. McKee before the Philadelphia Pediatric Society in June, 1903, the history of which is given in full by Dr. McKee in a preceding article, in the same number of this JOURNAL. The ophthalmoscopic appearances, seen first in March, 1903, were typical of the disease, and are well illustrated by Dr. Buchanan's sketches. Directly in the macular region of each eye there was a horizontally oval, white area, in the centre of which was a sharply defined cherry-red spot. The white area measured about two disks' diameter across, and faded off gradually into the surrounding retina. The fine retinal vessels were not veiled, and ran uninterruptedly across it. The optic nerves were in a condition of white atrophy, the arteries being especially reduced in calibre. Later examinations made by Dr. Buchanan showed a gradual reduction in the size of the white spot, which took the shape of a vertical instead of a horizontal oval, and became grayish in color, while the red spot assumed a brown hue. The lesion did not disappear entirely.

The child died of pneumonia at St. Christopher's Hospital, February 23, 1904, at the age of twenty-nine and one-half months. Permission to perform an autopsy was difficult to obtain, because of religious beliefs, and after eight hours 10 per cent. formalin was injected into each eye, to prevent, if possible, post-mortem changes.

<sup>1</sup> Read before the Section on Ophthalmology of the College of Physicians of Philadelphia, April 19, 1904.

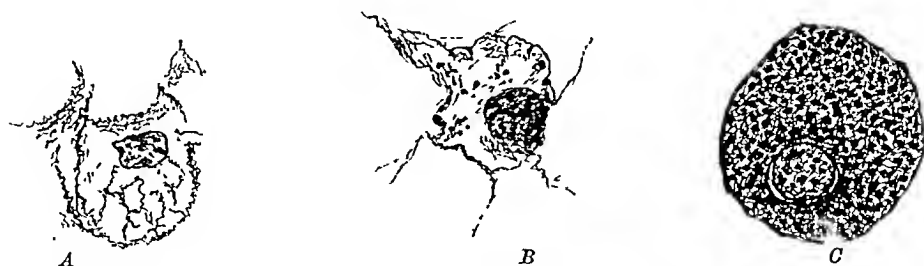
The autopsy was finally made nineteen hours after death. The eye-balls were removed entire; one was placed in 10 per cent. formalin and the other in Müller's fluid. The one placed in formalin was removed after twenty-four hours and hardened in ascending strengths of alcohol until 75 per cent. was reached. It was then divided in a horizontal plane, the section passing through the macular region, in which the discolored area was still visible macroscopically. Portions of the retina in this region were cut out and embedded in paraffin, so that study could be made of the ganglion cells. The other half was embedded in celloidin, and serial sections were cut and stained with hæmatoxylin-eosin, by the Van Gieson method, and with thionin. The eye placed in Müller's fluid, together with the optic chiasm, remained in this solution, with several changes into fresh fluid, for four weeks, and was subsequently hardened in alcohol, bisected, and embedded in celloidin for study of the changes in the optic nerve by the Weigert method.

The sections cut in paraffin pass directly through the macula and fovea centralis. They were stained with a 2 per cent. solution of thionin, for ten minutes, washed in water, differentiated in absolute alcohol, and mounted in xylol balsam. Microscopic examination shows the following conditions: Post-mortem changes are inconspicuous, and no œdema of the retina can be found. The ganglion cells, however, are in an advanced stage of degeneration. Many of them have disappeared completely, so that in the macula, where the cells are ordinarily present in rows of from three to six or even more, only a single, interrupted row can be seen. The cell bodies are so lacking in chromophilic elements, that they can be detected only in the very deeply stained, and slightly differentiated sections. Then the distorted nucleus is seen to be surrounded by a network which represents the framework of the cells. The cell outlines are irregular, in many cases rounded, and without any dendritic process. The Nissl bodies have disappeared entirely. Compared with the cells in the normal retina of a child they are swollen. In many cases the cell body has disappeared, leaving the nucleus alone. Sections of the Müller solution eye, stained by the Weigert method show the swollen cell bodies better, and reveal the presence of closely packed granules in the cell, which stain dark brown. Sketches made by Dr. Buchanan (Fig. 1) illustrate these changes very distinctly.

The retina, as a whole, is thinner than normal, and the thinning seems to be at the expense of each of the layers. The nerve fibre layer is narrower, the ganglion cells are reduced in number, as has been described, and those of the inner and outer nuclear layer, representing respectively the bipolar ganglion cells, and the nuclei of the visual cells, are also fewer than in the normal eye. Many of the former are irregular in outline, and show nuclear degeneration. The inner segments of the rods and cones are preserved,

but the outer segments are degenerated. This degeneration is possibly in part due to post-mortem changes, but not entirely so, as the sections show penetration of this layer, here and there by

FIG. 1.



Degenerated ganglion cells: *A* and *B*, stained with thionin; *C*, stained with Weigert stain.

clumps of the characteristic pigment granules from the retinal pigment layer. In the formalin eye, the retina has remained in place throughout, and the sections of the part removed for paraffin embedding show that the choroid is included with the retina,

FIG. 2.



Photomicrograph of the optic nerve at its entrance to the eyeball, showing entire atrophy of fibres on the nasal side, with some normal fibres on the temporal side. Weigert stain.

although the retina is ordinarily much more easily removed from the choroid than is the choroid from the sclera. In the macular region, the retina, in the celloidin sections, measures  $132\mu$ , while

in similar sections from a normal child's eye, hardened and embedded in the same way, it measures  $247\mu$ . The retina is therefore reduced almost one-half in thickness, and the adhesion of the retina and choroid, with the pigmentation of the outer layer, show that a decided atrophy, with adhesion between the retina and choroid must have been present during life. The sections of the optic nerve, stained by the Weigert method reveal an entire absence of normal fibres in its temporal half, and a great reduction in those on the nasal side; this part of the nerve, however, shows many normal fibres, as the photo-micrograph (Fig. 2) by Mr. Walmsley at the Pepper Laboratory demonstrates. Sections of the chiasm and optic tract show complete atrophy of all the nerve fibres.

In the 11 cases in which the anatomical examination has been made, the conditions present in the eyes have been recorded in only 5. The first 2 were Kingdon's cases, in which the eyes were examined by Treacher Collins,<sup>1 2</sup> who found œdema of the retina, especially located in the outer molecular layer, and atrophy of the optic nerves. At the time of these examinations, however, very little attention was paid to the study of the ganglion cells, and nothing is said specifically about their condition. Moreover, in both cases, the eyes were fixed in Müller's solution, so that the retinas were detached from the choroid and exhibited folds in the macular region. Müller's solution was shown to be a poor fixing solution for the retina by Schultze.<sup>3</sup> The membrane is inevitably detached, and its elements are distorted by the pulling of the shrinking vitreous humor. Very deceptive pictures of œdema are produced in this way, as is shown in a striking manner by comparison of the eyes in our case. In the formalin eye the retina is in place, and in the celloidin sections, measures  $132\mu$  in thickness at the macula; in the Müller solution eye the retina is completely detached, there is decided spacing out of the layers, and it measures  $336\mu$ , or nearly three times that of the retina in the fellow eye. On the other hand, formalin does not disguise an existing œdema, as examination of sections of eyes with detachment of the retina or high-grade optic neuritis will prove. We believe, therefore, that the findings of Collins were due in part to the fixing solution used, and to the deceptive appearances caused by the folds in the macular region.

In the third case (Peterson's) examined by Ward A. Holden,<sup>4</sup> the autopsy was not made until forty hours after death, so that the results were unsatisfactory, owing to the advanced post-mortem changes.

The fourth case (Hirsch's) was also examined by Holden.<sup>5</sup> He reported enlargement of the ganglion cells, which had become globular and had lost their chromophilic elements. The cells stained by the Weigert method showed coarse, black granules. The cell membrane and the cytoreticulum could be made out under a

$\frac{1}{18}$  immersion, but no Nissl granules were present, and the cell body had the appearance of having had its liquid contents withdrawn, leaving the naked cell framework.

Finally Mohr's<sup>6</sup> case, published in 1899, in which the eye was fixed in Flemming's chromic-osmic acid solution. Mohr reported œdema of the outer molecular layer, especially of the so-called Henle fibre layer, which makes up the outer portion of this layer, in the region of the yellow spot, a degeneration of the outer segments of the rods and cones, and the formation of a granular substance between the external limiting membrane and the choroid, which measured  $380\mu$  in thickness, although the retina itself in this region measured but  $70\mu$ . The thickness of the Henle layer was  $350\mu$  against  $170\mu$  normally found in the adult retina. These conditions Mohr ascribes to œdema, probably caused by angioneurotic disturbances, the result of pathological alterations in the cervical cord. Such a marked thickening of this region, however, if present during life, would be surely evident ophthalmoscopically, and as Higier<sup>7</sup> observes, if œdema were caused by such alterations in the cervical cord, we would see the same fundus changes in other forms of organic disease such as syringomyelia, amyotrophic lateral sclerosis, cervical spondylitis, etc. Mohr's findings suggest very strongly that the retina was cut obliquely in this situation, and that the marked thickening was due to this fact. He makes no mention of the condition of the ganglion cells, although Holden's results were known to him, as they are mentioned in the summary.

Our examination, therefore, confirms Holden's view that the essential changes in the eyes are degeneration of the ganglion cells of the retina, and of the nerve fibres of the optic nerves and tracts, which are genetically a portion of the central nervous system. The process is in a more advanced stage, but this is what we should expect, as the child lived about eight months longer than did Hirsch's patient, while the disease was first noted at about the ninth or tenth month in each. It seems more reasonable to explain the white area in the fundus as the result of the swollen and degenerated ganglion cells, which are present in much greater numbers in the macular region than elsewhere, than to conceive it as due to œdema of the tissue. As Falkenheim<sup>8</sup> says, two facts speak against the assumption of an œdema: in the first place the unchanging appearance of the lesion for months, and the absence of any veiling of the finer vessels in the area. Nor would this theory be incompatible with the gradual reduction in size of the area, which was noted in our case by Dr. Buchanan, as the disappearance of the ganglion cells by degeneration would make the spot less conspicuous. What the condition is which causes this intense and widespread degeneration of the nerve cells and fibres, is as yet undetermined. Sachs<sup>9</sup> was at first of the opinion that it was due to an arrest of development, but he has altered his views, and now believes,<sup>10</sup> with other



investigators that the condition is a true degenerative one, and that it occurs so early in life because of an imperfect development of the nervous system. In other words, he accepts Gowers' term of "abiotrophy" or essential failure of vitality, and thinks that this is present as an inherited condition in these unfortunate cases. This seems to be the best explanation offered, at present, to account for the facts. Why certain children of a family are affected while others remain healthy, and why the children of Jewish parentage are especially liable to the disease, are questions which still remain to be settled.

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## A PATHOLOGICAL STUDY OF AMAUROTIC FAMILY IDIOCY.<sup>1</sup>

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AMAUROTIC family idiocy is a disease that has been studied especially by American physicians. Falkenheim<sup>2</sup> after a careful examination of the literature has found 64 cases reported (1901), of these 47 were seen by physicians, 30 cases (24+6) occurred in America, 11 (9+2) in England, and 23 (14+9) on the Continent of Europe.

More recently (1904) Heveroch<sup>3</sup> has collected the records of 86 cases, of which 44 occurred in America.

B. Sachs was the first to recognize the clinical symptoms of amaurotic family idiocy, and gave the disease the name by which it is now known. It was subsequently shown that one symptom of

<sup>1</sup> Read in abstract at the meeting of the American Association of Pathologists and Bacteriologists, April, 1904.

<sup>2</sup> Jahrbuch f. Kinderheilkunde, 1901, p. 123.

<sup>3</sup> Abstract in Neurologisches Centralblatt, October 16, 1904, p. 948.

the condition had been previously recognized by Warren Tay, who described a case presenting "symmetrical changes in the region of the yellow spot in each eye of an infant."

In his earlier publication on this subject in 1887, Sachs supposed the disease to be due to peculiar changes in the cortical cells. Hirsch was the first to show that not only the cortical cells, but all the cells of the gray matter of the entire central nervous system were similarly affected.

I have had the opportunity to make a pathological study in a typical case of the disease that had been under the care of Dr. J. H. McKee, and had also been examined by me and others. I am much indebted to Dr. McKee for the pathological material. His necropsy notes are as follows:

"A piece of nerve was cut from the internal plantar; a piece of muscle from the flexor brevis digitorum.

"Thymus was small.

"Thyroid was well developed and presented a large isthmus.

"Pericardium: There was slight increase in the amount of the fluid.

"Heart: Both post-mortem and chicken-fat clots were found, but there were no valvular or endocardial lesions.

"Lungs: The left lung showed a massive catarrhal pneumonia of the lower lobe, and of the extreme posterior portion of the upper. The apex and free anterior border exhibited considerable emphysema. The basal portion of the lower lobe sunk in water. The right lung showed similar pneumonic changes in the lower and middle lobes.

"Pleuræ were free from adhesions or recent exudate.

"Peritoneum: Nothing abnormal was noticed, and there was no undue dryness.

"Appendix was very long and thin.

"Intestine: The small bowel exhibited intussusception (agonal?) at five places. The large bowel was small and collapsed.

"Spleen was slightly enlarged but not unduly dark. It presented no notch.

"Liver also was slightly enlarged, but remarkable in the fact that it presented none of the naked eye appearances of fatty infiltration.

"Kidneys: Nothing of interest was noticed macroscopically. Suprarenals were apparently normal.

"Lymph nodes: The peribronchial glands were enlarged and red, but the process was obviously an acute one. No caseous lymph nodes were noticed either in the thorax or abdomen.

"Brain: The subarachnoid fluid was much increased in amount. The meningeal vessels were intensely injected. The brain itself was very moist and heavy."

The results of my microscopic study are as follows:

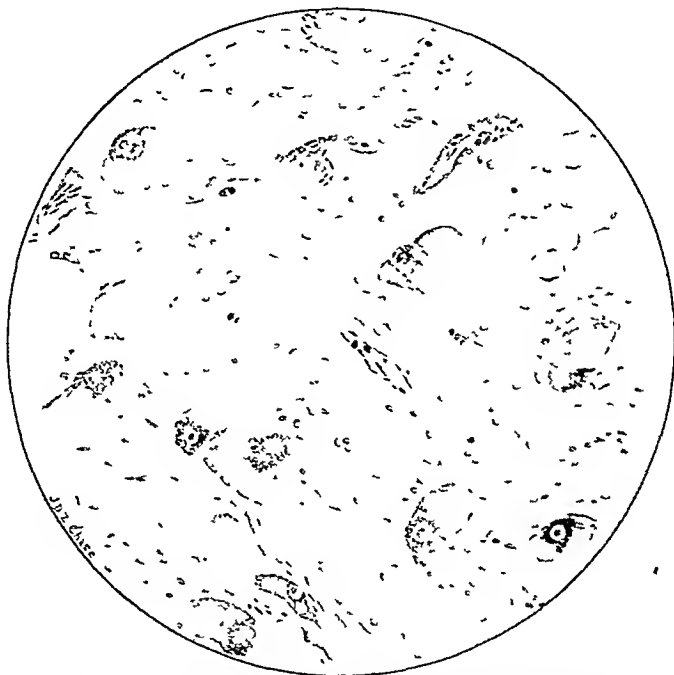
The nerve cells throughout the spinal cord are much enlarged, the chromophilic elements have disappeared except about the

nucleus, and here they have become granular, and in many cells the nucleus has been displaced to the periphery of the cell body. The dendritic processes of the nerve cells have disappeared in most of the cells.

The cells of the hypoglossus nucleus, of the nucleus ambiguus, of the lower olive, of the abducens nucleus, of the trigeminus and oculomotorius nuclei are in a similar condition.

The cells of Purkinje in the cerebellum are intensely altered, enlarged, and with the exception of the nucleus are structureless, so that they are found with difficulty.

FIG. 1



Cells of the anterior horn in the lumbar region in a case presenting the symptoms of meningitis. The pathological changes consist of an alteration of the nerve cells like that of amaurotic family idiocy. The cells are represented as they appear in one field of the microscope, in order to show the intense alteration of all the cells.

The nerve cells of the paracentral lobule, the small cells as well as the cells of Betz, and those of the frontal and occipital lobes are in a similar condition.

I have not been able to find a single normal nerve cell in the central nervous system.

The Marchi method shows most intense alteration of the white matter in the brain and cord, especially in the former.

The crossed pyramidal tracts do not contain black dots in the lumbar region, as the degeneration here is of long standing. The nerve fibres of the anterior horns show some degeneration by the Marchi method.

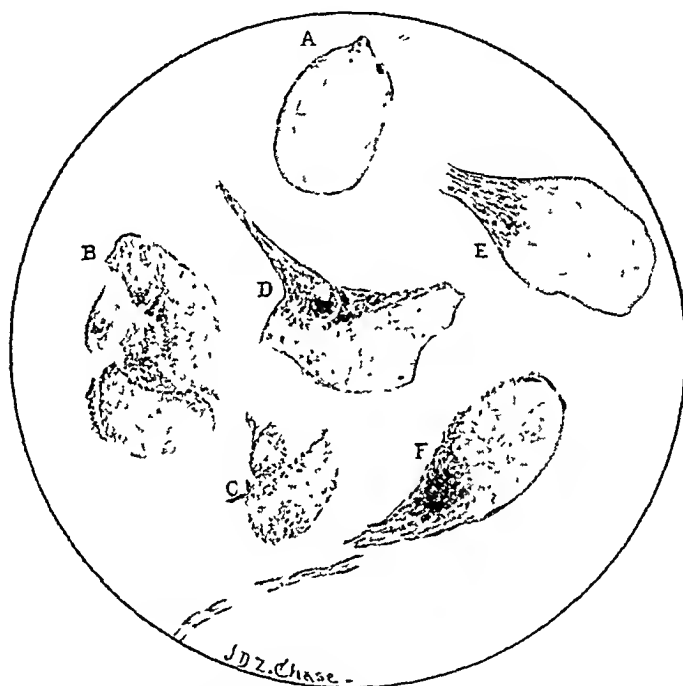
The crossed pyramidal tracts in the midthoracic region show a little recent degeneration, as do also the direct cerebellar tracts.

The same condition is found in the lower cervical region. The posterior columns are not degenerated.

The nerve fibres within the lower olives are much degenerated.

In the pons the intramedullary portion of the trigeminus, the lemniscus, the fibres crossing in the raphe, the superior cerebellar peduncle are much degenerated. The degeneration of the motor tracts is of longer duration than is that of many of the other tracts of the pons, but is still very intense, and much more so than is

FIG. 2.



Cells from the same case as represented in Fig. 1, selected from the anterior horns of the lumbar region, with the exception of cell *E*, which is from the paracentral lobule. Cell *A* shows complete chromatolysis. Cells *B* and *C* are broken into several fragments. In cells *D*, *E*, and *F* the chromophilic elements are seen only in one part of the cell body, and the nucleus is not distinct. By comparing Figs. 1 and 2 with the illustrations in the paper by Hirsch and Sachs it will be seen that the alterations are exactly like those of amaurotic family idiocy.

the degeneration of the pyramidal tracts in the cord as shown by the Marchi method. Indeed, an examination of the sections leads one to conclude that the motor tracts may have degenerated earlier in the cord than in the brain.

The foot of the cerebral peduncle is much degenerated, but the degeneration is of long duration, and is more intense in the dorsal portion of the foot, and here the fatty granular cells are very numerous, especially about the bloodvessels. There is comparatively little free degenerated myelin in the foot of the peduncle, and the numerous fatty granular cells stain deeply by the Marchi method.

This seems to indicate that the degeneration had existed long enough for the myelin to be absorbed by these cells.

Intramedullary fibres of the oculomotor nerve show a moderate amount of recent degeneration by the Marchi method.

The superior cerebellar peduncle is much degenerated and contains much free myelin.

The posterior longitudinal bundle may be slightly degenerated.

The lemniscus is considerably degenerated.

The white matter of the occipital and frontal lobes and of the paracentral lobule is much degenerated by the Marchi method.

Sections taken from the middle of the upper part of the corpus callosum are intensely degenerated by the Marchi method.

A piece of muscle from the foot, the flexor brevis digitorum, stained by the Marchi method shows no recent degeneration, but a piece from the same muscle stained by eosin and hæmalum shows an increase in the number of connective-tissue nuclei and probably also in the number of the sarcolemma nuclei. The muscle fibres appear degenerated, although I have no normal muscles from a child of about the same age for comparison.

A piece of one internal plantar nerve stained by the Marchi method shows considerable degeneration, but a piece from the same nerve stained by the Weigert hæmatoxylin method or acid fuchsin is not degenerated or at least very slightly degenerated.

Sections stained by the Weigert hæmatoxylin method or acid fuchsin also show degeneration of the central motor tracts. The anterior and posterior roots of the cervical and lumbar regions are not degenerated.

No signs of inflammation are found anywhere.

Falkenheim found that necropsies had been obtained in 11 cases; in 2, however, no report was made—those of Grosz. The 9 cases with reports of necropsies were those of Knapp and Sachs, Kingdon (3), Peterson, Hirsch, Mohr, and Clairborne. The report of necropsy in Clairborne's case is exceedingly brief. Since Falkenheim's paper appeared cases with necropsy have been reported by Frey (1), Schaffer (1), and Sachs (1). In Mohr's case the report of the histological examination was written by Schaffer.

Falkenheim says that in amaurotic family idiocy the degeneration of the pyramidal tracts has been followed through the cerebral peduncles, pons, medulla oblongata, and spinal cord. The lemniscus also has been found degenerated, as well as the tangential fibres, the spinal root of the fifth nerve, the anterior cerebellar peduncle, the columns of Goll, and the optic nerves. Falkenheim mentions Hirsch's paper, but he does not do justice to the latter's cellular findings.

Schaffer<sup>1</sup> found intense and widely diffused degeneration of the

<sup>1</sup> Wiener klin. Rundschau, 1902, p. 324.

brain and degeneration of the pyramidal tracts of the spinal cord. The gray matter of the cord was not diseased. No mention is made of the condition of the nerve cells of the brain. This is not the same case as the one described in Mohr's paper.

Frey's case is especially interesting because his is one of the very few in which the Marchi method has been employed in the study of a case of amaurotic family idiocy. He found increased consistency of the brain and spinal cord. The crossed pyramidal tracts, the tracts of Gowers, and the lateral border zones (*Grenzschichten*) were degenerated. The direct cerebellar tracts and the anterior columns were normal. The degeneration of the posterior columns, especially of the columns of Goll, began in the lower thoracic region and could be followed to the nuclei of the columns of Goll. The fibre reticulum of the anterior horns had almost disappeared in the cervical region. The white matter of the brain showed much degeneration. It is probable that the peculiar cellular alterations of amaurotic family idiocy were present in this case, although Nissl's method could not be employed. Frey<sup>1</sup> says that the pyramidal cells of the cortex were rounded and had lost their normal shape. There was no trace of inflammation. Evidently the peculiar cellular alteration of this disease escaped him, as he does not speak explicitly about it, and does not appear to have read Hirsch's paper. The optic tract and chiasm were degenerated but the optic nerves were normal. The entire central nervous system was affected.

He refers to another case of the disease that he was studying in which a pronounced degeneration of the nerve cells with vacuolation was found, but there seems to have been little to him that was characteristic in this cellular alteration.

Sachs<sup>2</sup> recent paper fully confirms the extraordinary cellular findings described by Hirsch in a case of amaurotic family idiocy, and these seem to be the only cases in which this peculiar and widespread cellular degeneration was reported, except that Sachs now believes that some of his earlier cases showed a similar alteration.

The description of the changes of the nerve cells in my report conforms very closely with those given by Hirsch<sup>3</sup> and Sachs.

If the widespread and intense cellular alteration is a common condition in amaurotic family idiocy it is remarkable that, according to Falkenheim, the electric irritability of the muscle is preserved, and that only Koplik and Grosz have found slowing or diminution of the faradic contractility.

Russell and Kingdon<sup>4</sup> stated in 1899 that no changes in the peripheral nerves had been found in amaurotic family idiocy, and

<sup>1</sup> *Neurologisches Centralblatt*, September 16, 1901, p. 836.

<sup>2</sup> *Journal of Nervous and Mental Disease*, 1903, p. 1.

<sup>3</sup> *Ibid.*, 1898, p. 538.

<sup>4</sup> *Allbutt's System of Medicine*, The Macmillan Co., 1899, vol. viii. p. 725.

I have not been able to find the report of any such changes recorded in the literature.

In the case that I have studied the piece removed from the internal plantar nerve was distinctly degenerated by the Marchi method.

I do not share Sachs' opinion that the changes in the nerve cells in the cases of Rolly, Collier, and Mya and Levi were like those of amaurotic family idiocy. Rolly<sup>1</sup> says that in the lumbar region the processes of the ganglion cells were abnormally intensely stained, and the portion of the processes that normally does not stain took the stain. The nerve cells were least altered in the lumbar region. Near ganglion cells that were entirely normal were others in which chromatolysis had occurred, in some this was perinuclear while the chromophilic elements at the periphery of the cell were preserved. Some cells showed peripheral chromatolysis while the chromophilic elements about the nucleus were preserved. Nowhere was there any marked alteration of the form of the cell.

The changes in the nerve cells of the thoracic region were like those of the lumbar region.

The changes in the cervical region were more intense. Normal cells were less numerous than elsewhere in the spinal cord, and chromatolysis was more pronounced. Still more intense were the changes in the brain. Nowhere does Rolly speak of a swelling of the cell, with destruction of the cell processes, and complete loss of all stainable portions of the cell except about the nucleus, which is displaced to the periphery. Nor was the alteration by any means found in all the nerve cells. The alteration of the nerve cells was pronounced in Rolly's case, but, as a study of his drawings show, it was very unlike that of amaurotic family idiocy. The pyramidal tracts were perfectly normal.

In two cases, one of cerebral diplegia and one of generalized rigidity, with necropsy reported by J. S. Collier,<sup>2</sup> the cellular alteration was not like that of amaurotic family idiocy. The pathological report in these two cases is by Risien Russell. In the first case there was a great paucity of nerve cells in the cerebral cortex. Neither the cells nor their nuclei presented any signs of swelling. Many of the cells preserved more or less their normal pyramidal shape, but they were all below the normal in size, many of them very much so. The cells stained diffusely by the Nissl method. The pyramidal tracts were degenerated.

In the second case the cellular alteration and the degeneration of the pyramidal tracts were very similar. The changes in the nerve cells in these cases were not at all like those of amaurotic family idiocy.

<sup>1</sup> Deutsche Zeitschrift f. Nervenheilkunde, Bd. xx. p. 152.

<sup>2</sup> Brain, 1899, vol. xxii. p. 378.

So far as I can determine the changes in the nerve cells described by Mya and Levi were not those of amaurotic family idiocy.

In 1899, in association with Dr. D.-J. McCarthy,<sup>1</sup> I reported a case not of amaurotic family idiocy, with changes in the nerve cells, however, like those occurring in this disease. The patient, a girl, was nine years old at the time of her death. Her sight was said to be good, but it is not known that any visual examination was made. She could not speak. She had a normal gait earlier in life. She began to walk before she was two years of age and had no motor paralysis. She never had convulsions. The feet and hands were always cold. She was said to be lacking in sensation, and would handle hot coals or hot food without making a sound of discomfort. She was exceedingly active and noisy, wet her bed and day clothing, did not understand what was said to her, and could not read. During the year previous to her death she showed gradual emaciation, but no cause could be detected for this. The gait was observed to be more shambling than previously. Emaciation became extreme before death.

At the necropsy the bridge of the nose was found flattened, the lower front teeth were nicked like those known as Hutchinson's teeth, the sternum was prominent. Internal hemorrhagic pachymeningitis was found on each side of the brain. The pia was very œdematous and the brain was quite soft. The nerve cells of the paracentral lobule, of the frontal lobe and posterior portion of the parietal lobe, of the cerebellum and bulbar nuclei, and of the anterior horns of the cervical and lumbar regions were swollen and altered in the manner described more in detail in the following case. The capillaries in the cerebral cortex and in the spinal cord were very numerous and congested. Secondary degeneration in the spinal cord was not present, even by the Marchi method.

These remarkable cellular changes throughout the central nervous system were described in detail and were represented by drawings. Reference also was made in that paper to the similar condition described by Hirsch in amaurotic family idiocy. Microscopic examination showed that in our case the optic nerves were normal. It was thought that the œdema of the cortex possibly might explain the alteration of the nerve cells, although it was acknowledged that the cases of uræmia reported in literature did not justify this view.

In 1900 I observed again changes in the nerve cells that were exactly like those occurring in amaurotic family idiocy in another case that could not be considered as typical of this disease. The patient, a boy, was within three months of eight years of age at the time of his death. The notes were incomplete, but it is recorded that he was of feeble mental development, did not know the alphabet, did not talk, and could not dress himself properly. His sight and

<sup>1</sup> Journal of Nervous and Mental Disease, November, 1899, p. 677. Spiller, *ibid.*, 1901, p. 140.



hearing were said to be good, although it is doubtful whether there was a visual examination. His gait was spastic. He was small and had scoliosis. Sensation was normal so far as could be determined. He did not have convulsions. He died with symptoms of cerebrospinal meningitis.

At the necropsy a large amount of cerebrospinal fluid escaped when the calvarium was removed. The brain was oedematous. The microscopic examination of the nervous tissues showed little evidence of inflammation. The nerve cells throughout the central nervous system were greatly altered, those in the posterior as well as those in the anterior horns of the spinal cord, the cells of the nuclei of the cranial nerves, sensory as well as motor, the cells of Purkinje and those in the parietal lobe, especially the cells of Betz, were all affected. The cell-body everywhere was swollen and rounded, many of the dendritic processes had disappeared; the chromophilic elements were seen only in one portion of the cell, and here they surrounded the nucleus, and even here they were more or less disintegrated, and the nucleus was at the periphery of the cell-body. Numerous small bacilli were found within the nervous tissues, but these may have entered the tissues after death.

In neither of these two extraordinary cases was secondary degeneration found, even by the Marchi method. Both children were of very feeble mentality, and were from the Pennsylvania Training School for Feeble-minded Children. It is incomprehensible that any function could be possible with such intense and general alteration of the nerve cells, and it is improbable that such an alteration could have existed a long time.

No one has been able to make a thorough microscopic study of the early degeneration of amaurotic family idiocy, and in those cases in which a microscopic examination has been made the disease had reached its full development and had been the cause of death. What the primary alterations are in this disease we do not know, but the widespread cellular alteration and comparatively slight changes in the white matter in the two cases referred to by me suggest that the cells probably are first diseased in amaurotic family idiocy, but this is by no means certain.

I cannot, any more than does Sachs, accept the view that amaurotic family idiocy is a toxic or acquired disease. Sachs, in referring to my second paper, remarks that I seem to interpret the cell changes as the result of the acute process in the cases to which I have referred above. The sentence to which he refers probably is this: "A theory of a toxic condition in the second case could be well supported by the clinical history, but not so well in the case of internal hemorrhagic pachymeningitis, although even in this it could not be absolutely rejected." I think I imply a very decided doubt regarding the nature of the process. Indeed, I feel unable to say why in the two cases to which I have referred such an extra-

ordinary pathological condition was found. These two cases are unique in the literature so far as I know, and, therefore, their interpretation at present should be left in doubt. They show a remarkable resemblance in their pathological findings to those of amaurotic family idiocy, and I am tempted to suggest that *possibly* they were aberrant types of this disease. In neither case was the clinical history complete and in neither case was an examination of the eye-grounds made.

It is important in this connection to mention that the first child to whom I have referred, who was the third child in the family, had a sister three years her senior, the second child in the family, who also died in a home for feeble-minded children, at the age of eight years, from what was supposed to be "tuberculous meningitis." It is very doubtful whether a microscopic examination or even a careful gross examination was made in this case. The two sisters were said to be so alike that the parents had only one photograph taken as representing both children. In my second case death occurred following symptoms suggestive of meningitis, and a number of children with amaurotic family idiocy have died with symptoms of meningitis.

Can there be a type of disease resembling closely amaurotic family idiocy but causing death about the eighth or ninth year of life, instead of within the second year of life? It seems to me that this is possible, because the alteration of the cells throughout the nervous system, in the two cases I have referred to, is entirely unlike anything occurring in other forms of imbecility and spasticity, and is so striking that anyone who has seen it once can never mistake it.

Russell and Kingdon say that two cases of amaurotic family idiocy have been reported in which death did not occur in the earliest years (they are those of Koller<sup>1</sup> and Peterson<sup>2</sup>), but Falkenheim remarks that these two cases were the same, so that really there was only one with a delayed fatal termination. The case is not with necropsy. Peterson mentions that in this case blindness was noticed when the child was six months old. At the time Peterson wrote his paper the child was five and a half years old and was an idiot. Falkenheim says that in 64 cases of amaurotic idiocy reported, death is mentioned as occurring in 38. Two patients died in the first half of the third year of life, one when three and a half years old, and the others before the end of the second year.

It is doubtful whether the case reported by Hirschberg<sup>3</sup> should be regarded as one of amaurotic family idiocy. His patient was fifteen years of age.

Falkenheim mentions that the characteristic ocular changes were

<sup>1</sup> New York Medical Record, 1896, p. 266.

<sup>2</sup> Journal of Nervous and Mental Disease, 1893, p. 529.

<sup>3</sup> Centralblatt für Augenheilkunde, January, 1904.

not found in all cases of amaurotic family idiocy, so that the uncertainty concerning the existence of ocular changes in my two cases is of less importance. The absence of ocular changes must make the diagnosis difficult.

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## A CASE OF CARCINOMA OF THE URETER APPARENTLY INDUCED BY A CALCULUS LODGED IN ITS JUXTAVESICAL PORTION.<sup>1</sup>

BY WILLIAM F. METCALF, M.D.,

AND

HOMER E. SAFFORD, M.D.,

OF DETROIT.

I. CLINICAL. The following case is presented largely for its pathological interest, some of its features being so extraordinary as to make some report of it scientifically imperative. The surgical treatment will be given in some detail, although, in the light of subsequent developments in the case, a different course would be pursued were a similar one again confronted. The safety of the measures adopted for relief is confirmed by the satisfactory recovery from the operation itself, while the failure ultimately to save the patient's life depended upon circumstances beyond my control.

The patient, Mr. J. H., aged forty-seven years, was admitted to Harper Hospital on October 29, 1903. His father had died, at seventy-six years, of Bright's disease; his mother was living. The maternal grandfather died of tuberculosis, as did also two maternal uncles. One maternal uncle died of epithelioma upon the face. One sister died in infancy; two brothers died of typhoid fever.

From the fourth to the twenty-fifth year of the patient's life he suffered frequent attacks of what he called "bellyache," more severe in the left side of the abdomen and radiating toward the testicle. It was said to be followed by a feeling of coldness in the centre of the abdomen. During his twenty-fifth year, he had a severe attack lasting from June until August, when the appearance of sudden relief was attended with a profuse discharge by the urethra. He was then free from pain for three years, at the end of which time occurred another severe attack of pain, lasting two days, and likewise followed by sudden relief. Two or three such attacks followed during the next ten years, and during the same interval he had occasional chills and fever.

September 1, 1903, he began to have severe cramping pain in

<sup>1</sup> Read before the Michigan State Medical Society (Surgical Section), Grand Rapids, May 26, 1904.

the centre of the abdomen, accompanied by nausea. This pain recurred at intervals until October 10th, when he suffered an attack more characteristic of renal colic. From this time until he entered the hospital, October 29th, it had been necessary to keep him continually under the influence of morphine. A marked scoliosis due to sympathetic muscular contraction was apparent. His pulse was 104, weak and compressible; the temperature 101°.

Dr. Lake, of Detroit, who had attended the patient for about two weeks before referring him to me, believed it a case of ureteral calculus. This diagnosis certainly best harmonized the facts of the case, but the positive location of the stone in any case cannot be made from the symptoms, and even under the most careful examination it is sometimes impossible to distinguish calculus ureteritis from other forms. In a tuberculous ureter a thickening may be mistaken for a stone, but the finding of tubercle bacilli in the urine would clear the diagnosis. Then the hæmaturia of tuberculosis is not relieved by rest in bed, as would generally be true of hæmaturia due to calculus.

Examination of the urine on admission to the hospital showed: specific gravity, 1008; reaction, alkaline; albumin, a faint trace; pus cells numerous, and an occasional red blood cell; many round and a few squamous epithelial cells; mucus, a small amount. With calculi in the kidney or ureter the urine is usually acid, regardless of pus and blood. Pus coming from the kidney produces a uniform turbidity, and this turbidity persists after the pus and mucus from a cystitis would have settled (Morris).

The tension of muscle over the kidney and in the loin was so great that I could not determine enlargement of the organ. The skiagraphic examination of the case was negative. The cystoscope likewise failed to render material service owing to the free hemorrhage arising from the interference of an enlarged prostate and the presence of a posterior urethritis. Furthermore, the patient's condition suggested the wisdom of proceeding without delay with the operation itself (November 2, 1903).

The beginning of the operation was by the lumbar incision for the purpose of exploring the kidney and the upper ureter. The wisdom of this procedure was confirmed by finding the kidney greatly enlarged and sacculated, it being distended with the retained purulent secretions. The thinning and atrophy of the parenchyma supported the clinical indications that the obstruction was complete, with occasional intermissions in which the obstruction became incomplete. Nephrectomy was immediately done.

After freeing the thickened ureter as far down as the finger could reach, I made an ilio-inguinal incision and stripped back the peritoneum. Then passing a long forceps upward under the attachment of the muscles to the iliac crest, I grasped the severed end of the ureter, dragged it out of the lower incision, and freed it

as far as its point of attachment to the bladder. In breaking up the adhesions about the ureter many little pockets of pus were opened, and the walls of the tube were the seat of considerable deposits of a friable calcareous substance, so that, in the effort to reach the vesical attachment of the ureter, it separated, leaving its ragged end bathed in pus and exposing a calculus.

Considering the rarity of malignant disease of the ureter and the dangers of prolonged operation in a patient so debilitated, it was thought advisable to delay any operative measures looking to the removal of the small remnant of ureter or other tissue left attached to the bladder. It was recognized that unless malignant disease was present no time would be lost by simply draining and approaching any benign neoplasm recurring later by way of the bladder itself. If malignancy were present, furthermore, the fact of the extension to the periureteral tissues, already possible, rendered the prognosis very uncertain. In the light of these considerations the wound was closed, allowing ample provision for drainage, both lumbar and inguinal. The patient reacted fairly well after the operation, and the symptoms of sepsis that had preceded it now gradually disappeared.

A reasonable improvement continued for about four weeks, when severe sacral pain began, to control which required large doses of morphine. The routine examination of the tissues from about the lower end of the ureter was reported from the laboratory as revealing an adenoma without malignancy; but later Dr. Safford, who undertook a careful histological examination of the case, found that, in the ureteral wall, in immediate proximity to the seat of the calculus, a decided and progressive malignant process was complicating the papillomatous and adenomatous changes, and that these latter seemed the results, more or less direct, of the irritating presence of the calculus. Attention was called to the fact that the primary, and as yet benign, steps in the process were to be found in the mucosa of the renal pelvis, which seems to permit the supposition that, owing to a more or less prolonged stay of the calculus in this location, the beginning had here been made toward what might likewise have ended in malignancy had not the source of irritation escaped from the kidney. The result of this irritation had, however, at no point attained to malignancy except in the lower ureter. Whether at this lower focus the stone directly set up the processes preliminary to malignancy, or whether these changes were induced by cells transplanted from the renal pelvis, is of minor importance.

The pain continuing to be intolerable, it was thought justifiable to attempt its relief, even though temporary, since by so doing the observation would throw further light upon the character of the growth. Accordingly, on the 26th of December, the patient was again anæsthetized and the exploratory cystotomy revealed

an essentially normal vesical mucosa. There was congestion and the ureteral orifice was open, as had already been evident in the effort to inflate the bladder for cystoscopic examination. The bladder was then carefully closed and the peritoneum opened. The cause of the pain was apparent; the neoplasm had extended beneath the peritoneum from the point of the ureteral separation to the promontory of the sacrum, which it covered. The greater part of the growth I removed from the spine, with the aim temporarily to relieve the pain, and in this I was not disappointed.

The patient, however, died January 20, 1904, apparently of exhaustion. Unfortunately, autopsy was not obtained.

The importance of this case is recognized when we find the writer of an exhaustive article recently appearing in the *Annals of Surgery* upon the "Surgery of the Lower Ureter" saying that primary tumor of the lower end of the ureter must be extremely rare, as he had found no recorded case. Ziegler's *Lehrbuch*, 1895, says in a very brief comment upon the tumors of the renal pelvis and ureter, that carcinoma may be the terminal event in a calculous pyelitis. Hektoen, reporting his case in 1896, says: "Recent works on surgery and on tumors contain no mention of carcinoma of the ureter." If we confine our observations to those carcinomata of the ureter the reports of which leave no doubt of their primary relation to that organ, a review of all would be necessarily brief. The most complete collection of cases of tumors of the kidney is that of Albarran, and from this collection there are five which leave little to question as to their primary origin from the ureter. Some others are apparently extensions from the renal pelvis by continuity or by being engrafted from growths in that location. One case, that of Hedenius, is, from the best report of it available, somewhat doubtful, though more probably arising in the renal pelvis. One, that of Davy, is for some reason not in Albarran's collection, but the report so strongly suggests the case herein reported that it should find its place in any enumeration of these tumors. I will mention briefly all of these cases in order better to allow judgment of the one I have described.

CASE I.—Reported by Jona. Male. Tumor described as an adenoid papillary epithelioma of the left ureter, discovered in the subject post-mortem. No satisfactory history. The neoplasm occupied a peculiar diverticulum from the lower portion of the ureter, of the size of a hazelnut, and was beginning to manifest infiltrating properties.

CASE II. Voelcker's case. Male, aged sixty-eight years. Hæmaturia four months. Pain across loins; nausea; villous carcinoma of lower two inches of left ureter. Metastasis of liver. Deeply infiltrated walls of ureter, with extension through upon its external surface.

CASE III. Wirsing and Blix. Female, aged forty-one years. Medullary carcinoma, first five inches of the ureter. Invasion of renal pelvis. Involvement of peritoneum and rectum. Hydro-nephrosis.

CASE IV. Hektoen. Female, aged fifty years. Increasing pain eight months. Right inguinal tumor, which seemed connected with right ilium. Bedridden-three months. Diagnosis, clinically, osteo-sarcoma. Post-mortem, medullary carcinoma of right ureter, lower end of lumen of which admitted probe only about 2.5 cm. Inner surface of ilium eroded. Right kidney reduced to a cystic cavity containing 800 c.c. of slightly turbid, grayish, thick fluid.

CASE V. Rundle. Male, aged forty-six years. Tumor, right side, one year before. Hæmaturia. Lumbar nephrectomy. Numerous cylindrical cells in fluid. Squamous epithelioma of lower part of ureter projecting into bladder. Growth within two inches of renal pelvis. Metastasis in liver and lungs and mesenteric glands. Hydronephrosis.

CASE VI. Davy. Male, aged fifty-three years. Pain, left loin, down side, and in penis for three years, and increasing for past seven months. Hæmaturia, intermittent. Calculus, size of pea, passed six months before. Tumor in left groin for two years, now fluctuating, not painful, immovable. Hydronephrosis, thirty-three ounces of fluid, emptied but refilled. Nephrectomy. Probe in ureter passed down four inches. Death two months later. Calcium oxalate calculus, size of hazelnut, in the mass of an encephaloid carcinoma which involved the base of the bladder and the rectum, but apparently had arisen from the ureter at the seat of the calculus. The rectum had ulcerated through.

CASE VII. The case herein reported.

It will thus be observed that in only one case beside our own, that of Davy, was the stone found *in situ* as the probable cause of the growth; although the history of hæmaturia, especially where that appears early in the case, would strengthen the importance of calculus as a factor. The possible relation of errors of development is illustrated in Case 1. Primary carcinoma is in the ureter evidently a disease of rather advanced life. In the cases cited the age ranges between forty-one and sixty-eight years. All but two of the cases reported were in males.

The cardinal symptoms as they appear early are, in the order of their importance, pain, hæmaturia, and tumor. At least the first two may appear independently. The tumor would usually be that of renal enlargement due to obstruction, although as appeared in Hektoen's case there may be early enlargement of the neoplasm itself.

In the diagnosis of primary carcinoma of the ureter little of a pathognomonic character is to be derived from an examination of the urine. By segregation of the urine it would be possible to find

blood or cells from which a growth could be determined as present in either the renal pelvis or the ureter on the side on which they were found, and by sounding the ureter the presence of an obstructing growth could be more or less definitely made out. Morris calls attention to the evenness of distribution of the pus coming from the ureter or renal pelvis and the consequent slowness with which it settles to the bottom of the retainer. The location of the growth is by preference like that of the lodgement of calculi in the ureter, at one of the extremities or at the point of passage of the ureter over the brim of the pelvis. The following from Henry Morris summarizes the situation concisely: "Even when the side is indicated and a tumor is diagnosed it is still impossible to say whether the disease is primarily of and limited to the ureter, or primarily of and limited to the renal pelvis, or whether both these sections of the excretory duct are involved." And "if with the cystoscope vascular fringes or a pedunculated tumor or an ulcerated thickening at the orifice of the ureter is detected, the symptom is pathognomonic and the diagnosis is conclusive of disease of the ureter; but it affords no evidence as to whether the disease is primary or secondary, innocent or malignant; even if typically innocent below, cancer may be situated higher up."

It goes without saying that the treatment of primary carcinoma of the ureter is operative, and, since the location of the growth in this organ should give pronounced symptoms relatively early, a considerable proportion of cases should allow a fairly favorable prognosis. As a matter of fact, in the cases recorded up to this time no treatment was directed to the condition itself owing to a failure to make an ante-mortem diagnosis. When it is recognized that the ureter may become the seat of primary changes of a dangerous and even malignant character, doubtless such diagnosis will more often open the way to successful treatment. In urging the possibility of malignant changes it should not be forgotten that there should be no trifling with those seemingly benign. The proportion of recurrences after the removal of apparently simple papillary growths from the urinary tract is large, and in the recurring neoplasm the appearance of malignant characters is not uncommon. In a case reported by Roux, where a simple papilloma was removed from the renal pelvis, recurrence was in the form of a medullary carcinoma appearing ten years later. Again, the case we herein present illustrates the danger attending the neglect of calculi in the kidney and ureter. This point is all the more urgent when we consider the relative safety of nephrolithotomy and of ureterolithotomy in competent hands. The ureter should always be sounded in any exploration of the renal pelvis for calculus.

For the removal of any growth from the ureter, except in those rare cases where the tumor located at the vesical orifice is accessible through an incision and approach by way of the bladder, the



lumbo-ilio-inguinal or ilio-inguinal incision will be chosen. The lumbar opening permits the better judgment of what disposition to make of the kidney. The sacral or vaginal approach in the female or the prerectal in the male would be a useful alternative in some cases where it was necessary to reach the vesical end of the ureter.

With a certain diagnosis of malignant disease of the ureter immediate nephro-ureterectomy is the only safe course. Even in cases of benign tumors, where a complete removal of the diseased tissue would not permit the satisfactory approximation of the parts or the implantation of the ureter into the bladder, the same course is imperative. The suggestion of the implantation of the ureter into the intestine does not seem practicable in the light of our present experimental knowledge on this subject.

Where the region of the vesical attachment of the ureter cannot be absolutely freed from diseased tissue, Albarran, Morris, and others agree in advising an effort at its complete removal by way of the suprapubic incision, if necessary, at a subsequent operation.—W. F. M.

II. PATHOLOGICAL. 1. *Kidney*, with a small portion of ureter attached, removed at the first operation upon Mr. J. H., November 2, 1903. The kidney measured when removed 19 cm. by 13 cm. by 8 cm. Calices distended at the expense of the kidney substance by a thin, grayish purulent fluid until, with the exception of one wedge of relatively healthy tissue, the wall had a thickness of 0.5 mm. to 3 mm., and seemed on the point of bursting through at the thinner portions. Some tubular tissue remained in most of these thinner places, although under the mucosa was a deposit of old and recent inflammatory products. There were through the tissue cloudy swelling, hemorrhages, and many hyaline deposits. The wall of the lower renal pelvis was thickened, and in patches both here and in the calices the mucosa was velvety, with fine villous projections 0.2 mm. to 0.5 mm. in length. Areas covered with these fine villi were interspersed with others having ordinary transitional epithelium. Most of the villi here were simple or slightly branched, only occasionally one having an arborescent character and none so elaborately branched as the villi to be described in the lower ureter.

Covering these villi was an epithelium the outer layer of which was made up of rather long, pale-staining cylindrical cells with fairly deep-staining nuclei. In most of these villi there were underlying shorter cells, but in places the epithelium was thinned to a single layer of these long cells. Toward the base of the villus the single-celled arrangement was common where it seemed to be continuous with that of the cuboidal cells of the renal tubules. The villi of the renal pelvis usually presented a slender connective-tissue support or core.

The picture here presented is one not uncommon in villous pyelitis; but attention is directed to the tendency toward a meta-

FIG. 1.



Mucosa of renal pelvis. Transitional epithelium undergoing change to columnar. Magnified 30 diameters. (Dr. W. H. Knap.)

FIG. 2.



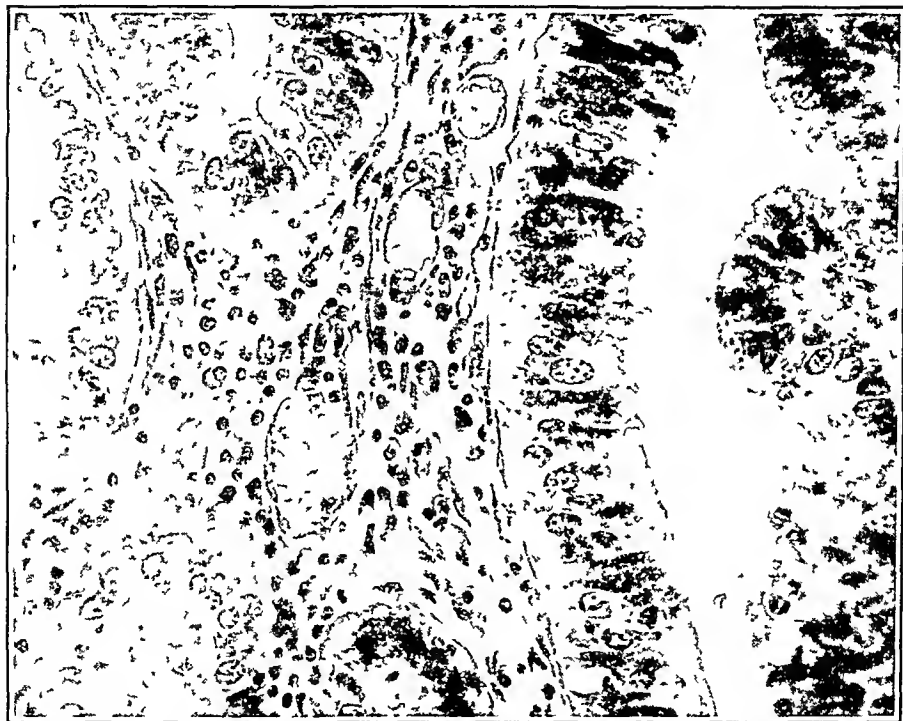
Mucosa of renal pelvis. Papillæ with columnar epithelium. Transitional epithelium with metaplasia to a columnar type. Magnified 65 diameters. (Dr. P. M. Hickey.)

plasia from the ordinary transitional epithelium lining the pelvis toward a single-celled columnar type. The kidney as a whole was

found in a condition of pyonephrosis; the portion of relatively normal tissue remaining confirms the intermittent character of the nephrectasis.

2. *Ureter.* (a) The portion left attached to the kidney just described. Diameter at the point of narrowing just below the renal pelvis was a little less than 1 cm.; the abnormal thickening involved all the coats. The lumen was open and distended with pus. In the thickened mucosa are numerous radial clefts extending one-half to two-thirds of the way through the transitional epithe-

FIG. 3



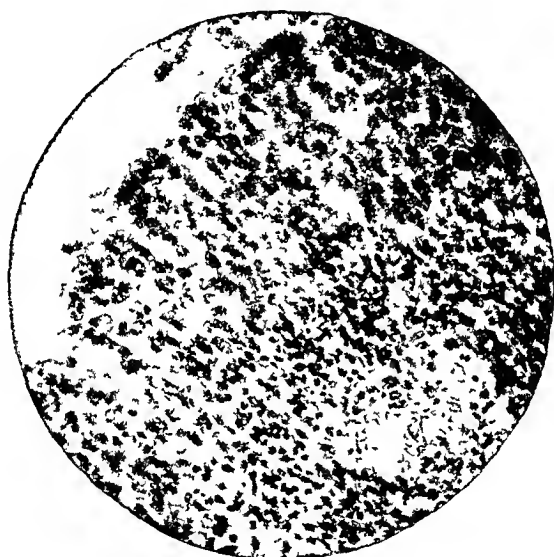
Mucosa of renal pelvis    Altered epithelium covering papillae    Magnified 350 diameters  
(Dr. W. H. Knap)

lium, marking it off into roughly cuboidal portions, underneath which there is an increased proliferative activity of the connective tissue, as well as a decided increase of blood supply.

(b) The next section is taken at a point about 15 cm. above the bladder, where the diameter was 1 cm. It may here be observed that from this point downward the ureter increases progressively in diameter until at the lowest point at which it is intact it measures 2.5 cm. by 3 cm. The remaining portion, about 1 cm. in length, includes a frayed-out end, where a new-growth surrounding a calculus had been separated in the effort to remove it. The

lumen, circular in the upper portions, becomes crescentic at the point 2 cm. or 3 cm. above the lower extremity by reason of the upward extension of this new-growth. The naked-eye appearance, as well as that under the microscope, is more and more remarkable as we pass downward. The clefts become deeper, the submucous proliferation is more active, and the result is that the lumen is surrounded by a row of cuboidal gross divisions covered over with tongue-shaped projections from the modified transitional epithelium. One striking change, the beginnings of which are to be seen in the section described above (*a*), is the alteration in form in the superficial layer of cells of the transitional epithelium toward a distinctly columnar type, with long pale-staining cylindrical cell-body

FIG 4.

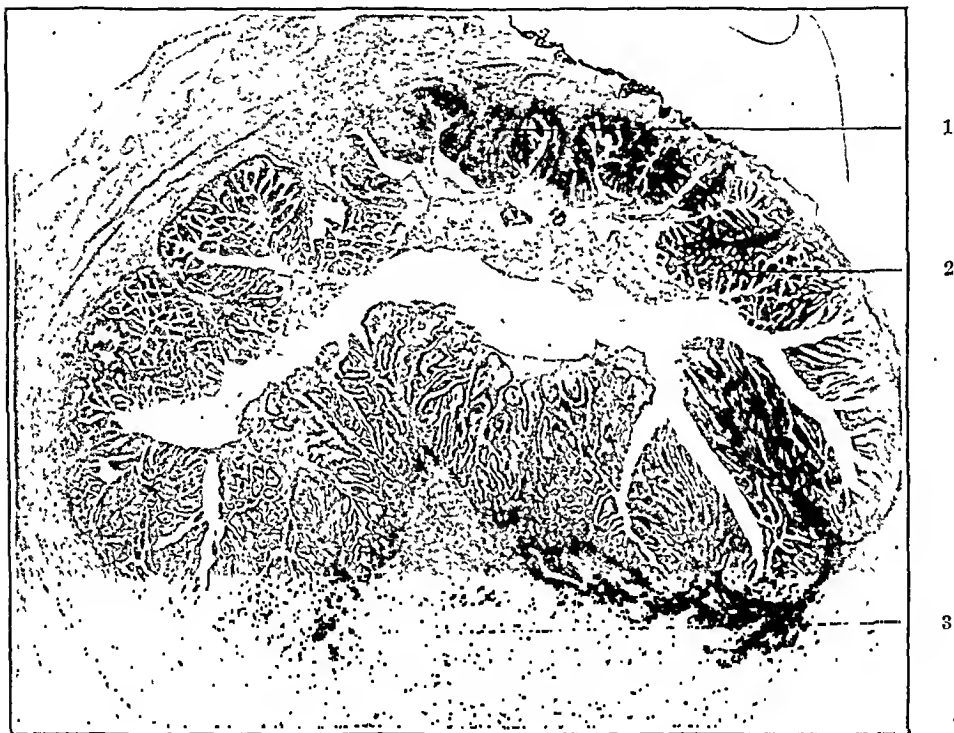


Mucosa of upper ureter. Formation of clefts Beginning of change of transitional epithelium to columnar type Magnified 200 diameters. (Dr. P. M. Hickey)

and rather deep-staining nucleus removed to the end of the cell toward the basement membrane. It seems to be the same change, in less marked degree, as is present in the papillary areas described in the kidney pelvis. Along with the change to a columnar form of the cells, the multiplication of the clefts, themselves lined with these same columnar cells, and the submucous proliferation, there comes a thinning out of the deeper layers of the stratified epithelium. The end-product of this change seems to be the condition found in the next section, (*c*), where the main divisions become the trunk and the subsidiary papillary processes the branches of the elaborate arborescent villi there seen. In the deepest layer of the transitional epithelium, the cells often show an unusually pronounced columnar character illustrating the apparently general tendency.

(c) This section was taken 3.5 cm. above the bladder. While in the previous sections the proliferation of the submucosa and the epithelium has thrown the wall of the lumen into an unusual number of broad folds, and the epithelial increase has aided the formation of the finer villous processes, we here find the mucosa, now thinned to a single layer of tall cylindrical cells, covering the arborescent villi just mentioned. These extend from 1 mm. to 2.5 mm. out from the wall into the lumen, and each has a well-

FIG. 5.



Cross-section of ureter, 2.5 cm. from bladder, 1 cm. below section (c) described in the text, and somewhat above the section described at (d). 1. Papillary processes covered with transitional epithelium. 2. Arborescent villi extending over the area of adenocarcinoma at 3. Magnified 8 diameters. (Dr. W. H. Knap.)

developed connective tissue support or core. Twelve or thirteen of these large villi surround the lumen, and the circle is completed by the presence at one side of two broader, less prominent papillomatous folds like those in the last-described section. These folds, in the same way, are covered with transitional epithelium traversed by the same radial clefts, and otherwise similarly altered. The apparent transition between these two kinds of epithelium, as well as the fact that so small a portion of the circumference is left covered by the form found in the sections above, seems to indicate an active progress of the change here found.

The picture of this arborescent villous growth is, in section, that of a simple adenoma which stands in apparently a transitional relation between the papillomatous hyperplasia of the sections above and the malignant tissue product observed in the next section. It is interesting to note that upon the side of the arborescent villous next to the broader folds above described the transitional epithelial covering of the latter rises to a little distance from the base, as though the process of transformation were incomplete.

(*d*) This section, taken across the ureter just above the point of lodgement of the calculus, shows the arborescent villi arranged, as in (*c*), about the lumen, here crescentic, while upon the opposite thickened wall none of these appear. At the edge of this thickened portion, which is the section of the upper end of the cancerous

FIG. 6.



Adenocarcinoma of the ureter, juxtavesical portion, in proximity to calculus. Showing change of gland-like processes at base of arborescent villi to carcinoma. Magnified 65 diameters. (Dr. P. M. Hickey.)

mass, there may be found, in continuity with the cylindrical-celled epithelium covering the arborescent villi, more or less definite gland-like extensions of the epithelium downward toward the muscular structures. By the abnormal proliferation of the cells of these gland-like processes, however, the epithelial arrangement is soon lost, and there is left only the more or less rounded areas of cancer cells divided by the intervening stroma. The grades in this transition are easily traced at the advancing line of the neoplasm. The cells are altered in form by the compression induced by their rapid growth, and the nuclei are less deeply stained, but the steps in this process are evident.

We may then speak of the condition in the lower ureter in immediate proximity to the seat of the calculus as adenocarcinoma,

primary in this location and medullary in character. There seems little question of the etiological relation of the calculus by reason of its long-continued irritation. Almost as conclusive is the evidence that the papillary changes, more and more pronounced as the seat of the calculus is approached, as well as the adenoma, apparently representing an intermediary wave of influence, are only the more remote effects of the same irritating cause.

The condition observed in the mucosa of the renal pelvis, tending toward the same adenomatous change, finds its place then as another step in the process, probably likewise induced by the irritating presence of the calculus before its escape into the ureter and checked in its course by the latter event. The alternative of accounting for the adenomatous condition in the ureter by the development of isolated remnants of the Wolffian body or hypothetical glandular structures is given less weight both by reason of this change in the kidney and the metaplasia toward a simple columnar epithelium from the normal transitional type observed in both organs. One other possibility suggests itself, viz., that the adenoma seen in the ureter has resulted from the engrafting upon the ureteral mucosa of correspondingly changed cells cast off from the lining of the renal pelvis; but this in no way alters the aspect of the case so far as the metaplasia is concerned, and it is as easy to believe that the whole process could follow the same influences at the lower focus.

3. *Tissue removed from behind the bladder* at operation, December 26, 1903, showed the same irregular, encephaloid mass of cells in groups separated by bands of stroma as were seen in the primary tumor.

4. *Calculus* of calcium oxalate weighing 1.25 grams and measuring 17 mm. by 9.5 mm. by 8 mm. Its surface is roughened by fine but rather sharp projections. In general its form suggests that of an olive stone. It is very hard, and in section there are to be seen concentric layers of a grayish-brown color.

It should be observed that calcium oxalate calculi are the ones most apt to be associated with tumors of the ureter and the renal pelvis.—H. E. S.

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## PRIMARY SARCOMA OF THE BLADDER.

WITH A REPORT OF THREE CASES AND REVIEW OF THE LITERATURE.

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AFTER a careful review of the literature on the subject the author has been impressed by the fact that sarcoma of the urinary bladder, as compared with other tumors of this viscus, is of decidedly uncommon occurrence. As an illustration of its infrequency the following expressions from some of the recent editions of our American text-books on pathology are quoted: "Sarcoma of the bladder is very rare;" "Sarcoma (of the bladder) has been described," etc. In some of the works consulted no reference is made to the subject.

Senftleben<sup>33</sup> receives the credit for having recorded the first case of this disease in 1861, the specimen having been examined by Billroth and pronounced sarcoma by him. Since then a considerable number of cases have been reported, but as in some of the reports the result of a microscopic examination is not given, and as some of the specimens were old museum specimens, the diagnosis may in part of the cases be questioned. It will be noted that the majority of the cases have been reported by English and German observers. In this country cases have been published by Stimson,<sup>26</sup> Musser,<sup>18</sup> Weir,<sup>45</sup> Krouse,<sup>28</sup> and Bunce.<sup>29</sup> W. R. Williams,<sup>4 5</sup> (1882-83) receives the credit for having recorded the greatest number of cases, 6 in all, 3 of which were specimens in the museum of the Middlesex Hospital. In reporting a case in 1888, D'Arcy A. Power<sup>19</sup> mentions 9 cases in all of sarcoma of the bladder preserved in the museums of the London hospitals. At as recent a date as 1884 Sir Henry Thompson stated: "The existence of true sarcoma of the bladder has been confirmed, but not on the observation of fresh specimens." In 1890 the same author,<sup>8</sup> in recording a series of 41 cases of vesical tumors operated by himself, speaks of three of them as being sarcoma.



No.	Date.	Name.	Sex and age.	Symptoms and their duration on seeking medical advice.	Location, gross appearance of neoplasm, etc.	Microscopic examination.	Remarks.
1	1861	Senftleben,	F. 29	Cystitis for one year.	Right side of fundus near ureteral orifice.	Spindle-celled sarcoma.	Growth partially extirpated; death from peritonitis.
2	1875	Gussenbauer,	M. 12	.....	Posterior wall; size of fist.	Myosarcoma.	Section lateralis et sectio alba.
3	1878	Stimson,	M. 63	Cystitis with hæmaturia and strangury for three months.	Posterior wall four inches above neck of bladder.	Sarcoma.	Not operated; death in three to four months.
4	1878	Marchand,	F. 57	Cystitis for two years.	Posterior wall near trigonum; size of small apple.	Round-celled sarcoma.	Not operated; death from exhaustion.
5	1879	Henth,	F. 39	Cystitis for seven years; strangury.	Left side; villous appearance; secondary growth attached to left innominate bone.	Round-celled sarcoma (medium sized).	Not operated; death in seven years.
6	1879	Heim-Vogtlin,	F. 56	Cystitis for two years with strangury and hæmaturia.	.....	Fibrosarcoma.	Extirpation; death one year later.
7	1881	Slevert,	F. 8	Cystitis followed by purulent peritonitis.	"Good sized;" anterior wall extending through urethra into vagina.	Round-celled sarcoma.	Several operations; death.
8	1881	Musser,	M. 50	Frequent micturition for five years; occasional slight hæmaturia.	Flat growth in trigonum involving both ureteral openings; surface irregular, in some places ulcerated.	Sarcoma.	Not operated; death from exhaustion in eight years.
9	1882	Butlin,	F. 3	.....	Entire bladder; red fungus growths; dendritic.	Round-celled sarcoma.	
10	1882	Williams,	F. 50	Cystitis for two years; anæmia.	Fleshy, reddish-brown, fungoid growth, size of hen's egg; vicinity of left ureter irregular, lobulated, and some ulceration.	.....	Not operated; post-mortem report.
11	1882	Williams,	M. 66	Cystitis for one and a half years.	Entire bladder invaded by flat, soft, purplish-brown growth; raised and knotty appearance; superficial ulceration.	.....	Median cystotomy; death from shock.
12	1882	Williams,	M. 52	.....	Posterior wall; irregular lobulated mass size of fist; short, broad pedicle.	.....	Not operated; post-mortem report.
13	1883	Williams,	M. 62	Frequent micturition; strangury; small stream; hæmaturia.	Soft fleshy growth, size of an apple, involving a diverticulum of bladder and left ureter; broad base.	Round and spindle-celled sarcoma.	Not operated; death.
14	1884	Eve,	M. 68	Hæmaturia, cystitis, and pain in loins for two years.	Anterior and upper walls completely lost in mass of new tissue; firm, pale, fibrous in places.	Lymphosarcoma.	Not operated; death from exhaustion.
15	1884	Eve,	...	.....	Vicinity of right ureter; ulceration.	Spindle and round-celled sarcoma.	Not operated; death from exhaustion.
16	1885	Fenwick,	M. 8	Profuse painless hæmaturia for six months.	Entire bladder covered with polypl. size of a cherry to a small plum, involving both ureteral openings.	Fibrosarcoma.	Perineal cystotomy; removal by scissor-forceps; death 6 months later from hæmaturia and exhaustion.
17	1885	Morgan,	M. 8	Always had difficulty in passing urine; no hæmaturia.	Springing from neck of bladder and involving base and vicinity of both ureteral orifices.	Lymphosarcoma.	Cystotomy; death from peritonitis.

18	1885	Chaffey,	M.	Difficult micturition and strangu- ry for 1 yr.; no hæmaturia.	Anterior wall behind pubes; portions were soft and crumbling.	Round and spindle- celled sarcoma.	Not operated; death from peri- tonitis.
19	1885	Schlegftendal,	F. 42	Incontinence; cachexia.	Posterior wall; tumor "good sized."	Spindle-celled sarcoma.	Colpocystotomy; patient dis- charged two weeks later; no further history.
20	1885	Langton,	M. 25	Hæmaturia for one year.	Base of bladder, left side; partly sessile, partly pedunculated.	Alveolar sarcoma.	Perineal cystotomy; extirpation; left hospital in good condition; no further history.
21	1886	Weir,	M. 55	Frequent micturition for two years; severe hæmaturia.	Posterior to orifice of left ureter; reddish friable growth two inches long, attach- ment three-fourths inch in diameter.	Sarcoma.	Cystotomy; removal by curette; recurrence six months later.
22	1886	Shattock,	M. 55	Hæmaturia and irritation for four years.	.....	Chondrosarcoma.	Operated by Thompson; peri- neal cystotomy; removal by forceps; recurrence.
23	1886	Chiari,	M. 5	Retention, hæmaturia, ascites several weeks.	Lower third of bladder.	Spindle-celled sarcoma.	Not operated; death from col- lapse and hæmaturia.
24	1886	Baker,	M. 55	Strangury for six months, hæmaturia two weeks.	Anterior and lateral walls and fundus; size of orange, cauliflower appearance; rectum involved; metastases in pleura and liver	.....	Suprapubic cystotomy; partial extirpation; recurrence; death three months later.
25*	1887	Thompson,	M. 55	Strangury with frequent mic- turition four to five years; hæmaturia one and a half years.	Upper part of bladder; large soft growth.	Round-celled sarcoma.	Cystotomy; removal of growth; death three months later.
26	1887	Jackson,	M. 76	Hæmaturia and frequent mic- turition for two years.	Base occupying trigonum and extending forward to prostate.	Alveolar, round-celled sarcoma.	Not operated; death in two and a half years.
27	1887	Wechselbaum	F. 36	.....	Base involving orifice of left ureter.	Giant-celled sarcoma.	Death.
28	1887	Power,	chd 4½	Strangury (extreme) eight weeks.	Anterior wall; irregular, lobulated, pe- dunculated.	Alveolar sarcoma.	Not operated; death in eight weeks.
29	1888	Lostalot,	M. 47	Strangury and frequent mic- turition; no hæmaturia.	Near neck of bladder.	Small round-celled sar- coma.	Death.
30	1888	Nicolich,	M. 47	.....	Fundus, especially anterior wall.	Myosarcoma.	Not operated; death.
31	1889	Golding-Bird,	F. 55	Cystitis; hæmaturia.	Growth moderately firm and vascular; pedunculated.	Sarcoma.	Suprapubic cystotomy; death four days later.
32	1889	Whitehead,	M. 46	Occasional hæmaturia lasting from several weeks to four months, for five years; in- continence.	Base, posterior and right lateral walls; soft diffuse growth; villous appearance.	Lymphosarcoma.	Perineal and suprapubic cystot- omy; extirpation; discharged as cured; no further history.
33	1889	Dittrich,	M. 1¾	.....	Fundus, submucosa and muscularis in- vaded; no metastases.	Spindle-celled sarcoma.	Post-mortem report.
34	1889	Dittrich,	F. 25	.....	Base; metastases in sacral glands and peritoneum.	Round-celled sarcoma.	Post-mortem report.
35	1889	Hinterstoisser,	M. 21	Profuse hæmaturia; retention; cachexia.	Anterior wall; cauliflower appearance.	Spindle-celled sarcoma.	Partial extirpation; death three months later from hæmaturia and exhaustion.

\* A second case reported at the same date by Thompson was previously reported (1886) by Shattock

No.	Date.	Name.	Sex and age.	Symptoms and their duration and on seeking medical advice.	Location, gross appearance of neoplasm, etc.	Microscopic examination.	Remarks.
36	1889	N. L. Univ. Hosp. Rpt.	M. 75	"Urine thick" for three years; frequent micturition; cystitis	Ragged growth $4\frac{1}{2}$ inches in diameter on right side; smaller growth $1\frac{1}{2}$ inches in diameter below orifice of left ureter.	.....	Not operated; post-mortem report.
37	1891	Hinterstolser,	M. 52	Hæmaturia and strangury four and a half months.	Right side of fundus and posterior wall, involving orifice of right ureter; size of walnut; calculus present.	Sarcoma.	Epi-pleystomy for calculus; death three months later.
38	1890	Bernstein,	...	.....	.....	Round-celled sarcoma.	Cystotomy; death from peritonitis.
39	1891	Skifosowski,	M. 23	Strangury followed by hæmaturia; painful erections; incontinence; anemia; pain in bladder nine and a half mos.	Size of man's fist, involving orifice of left ureter.	Alveolar, round-celled sarcoma.	Suprapubic cystotomy; removal by scissors and eurette; death three months later.
40	1892	Alharran,	ehd	.....	Neck of bladder and trigonum.	Myxosarcoma.	Death.
41	1892	Alharran,	$4\frac{1}{2}$	Cystitis for two months.	Neck of bladder.	Myxosarcoma.	Death.
42	1893	Frölich,	F. 4	.....	.....	.....	Death.
43	1893	König,	M.	.....	Neck of bladder; size of hen's egg; pedunculated.	Round-celled sarcoma.	Perineal cystotomy.
44	1894	Stankiewicz,	M. 35	Recurrent attacks of hæmaturia for eight months.	Posterior vesical walls; size of cherry.	Fusiform-celled sarcoma.	Suprapubic cystotomy; extirpation; no recurrence one year later.
45	1894	Steinmetz,	M. $2\frac{3}{4}$	Frequent micturition and strangury for three weeks.	Base of bladder; size of an apple.	Spindle and round-celled sarcoma.	Not operated; death in three months.
46	1895	Lohr,	M. $3\frac{1}{2}$	Irritation of bladder, incontinence, and hæmaturia for five weeks.	Posterior wall: size of pigeon's egg.	Small-celled sarcoma.	Settled alba; improvement; no further history.
47	1896	Krouse,	M. 52	Hæmaturia for six years.	Right side of neck, involving trigonum; sessile, irregular, firm, $\frac{3}{4}$ inch high.	Large round-celled alveolar sarcoma.	Suprapubic cystotomy; extirpation; recurrence of symptoms; death by suicide.
48	1898	Krouse,	M. 43	Hæmaturia and strangury.	Base of bladder; soft, size of child's fist, consisting of numerous lobes; calculus present.	Small round-celled sarcoma.	Suprapubic cystotomy; recurrence in three weeks.
49	1900	Bunce,	M. 14	Hæmaturia, severe strangury, retention for a few days.	Greater part of bladder and most of pelvis; large infiltrating mass.	Spindle and large round-celled sarcoma.	Perineal cystotomy and drainage; death a few months later.
50	1902	Paget,	M. 42	Hæmaturia for three months; anemia.	Base of bladder; size of hen's egg; sessile.	Round-celled sarcoma.	Suprapubic cystotomy; removal by cutting-forceps; recurrence and second operation in one year; left hospital in good condition one month later; no further history.

The diagnosis was confirmed by microscopic examination I judge in two of these cases, one of them having been previously reported by S. G. Shattock.<sup>46</sup> F. A. Southam,<sup>10</sup> in 1888, although he reports no cases of his own, writes an interesting and instructive review of the subject. He collected 34 cases claimed to have been sarcoma by different authors, but in some of the cases, however, proof of the nature of the growth seems to be inconclusive. H. Hinterstoisser,<sup>15 16</sup> in 1890, collected 32 cases and reported two of his own with microscopic examination. In the preceding table I have endeavored to collect those cases published in which there seems to be reasonably good proof of the diagnosis, with such data pertaining to them as was obtainable, and to present them in chronological order.

I have had the opportunity of making the diagnosis of sarcoma of the bladder microscopically in the following 3 cases: Cases I. and III. were attended by Dr. Leonard Freeman, of Denver, and Case II. by Dr. Sherman Brown, of Denver. To these gentlemen I am indebted for the clinical histories of the patients and the privilege of reporting them.

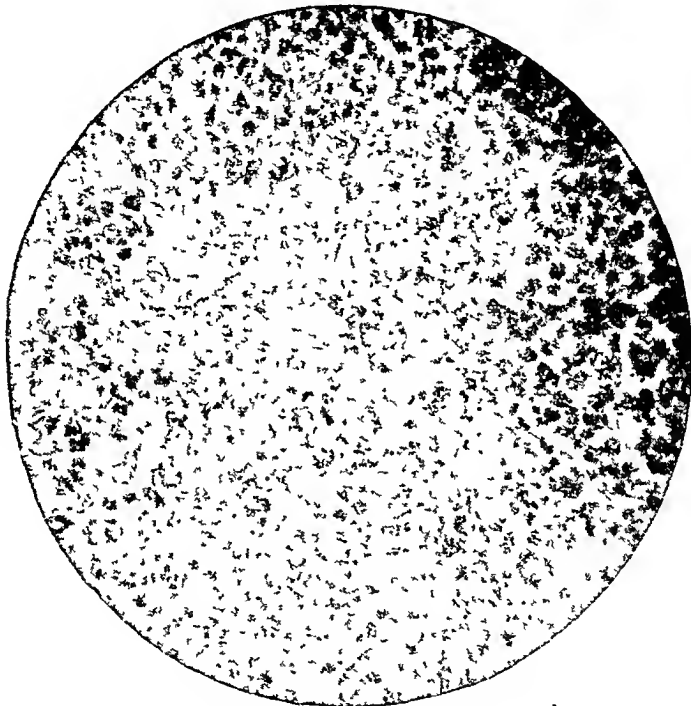
CASE I.—Male, aged forty-eight years; emaciated. Gives symptoms of bladder irritation extending over a period of five years. First attack of hæmaturia occurred about a year ago. Since then has had several attacks at irregular intervals. Complains of great pain on urinating and is obliged to urinate frequently. Urine has a fetid odor and is loaded with pus; no casts were found. Examination shows a stricture of the deep urethra; the bladder is very tender. Bladder opened by perineal incision, and a sessile tumor the size of a silver dollar at its base was found on the left side of the fundus near the neck. The growth was soft and friable, and consisted of projections resembling the “ends of fingers bunched together.” Some of these projections were easily scraped off with the finger-nail and saved for examination. The bleeding following their removal was readily checked by the use of hot water. No calculus was present. An attempt to remove the growth was not thought advisable. Drainage and irrigation relieved the patient of his bladder symptoms, but death occurred from exhaustion about six weeks later.

*Microscopic Examination.* Specimen presented for examination measures 3 x 1.5 x 1 cm., has a light flesh color, and is rather friable. Tissue hardened in formalin and alcohol, embedded in celloidin and stained by the usual methods. The sections consist almost entirely of cellular material, a few strands of delicate connective tissue being seen scattered irregularly through the specimens. The cells vary a great deal in size, the smallest measuring from 5 to 6 $\mu$  in diameter, a few of the largest measuring from 35 to 38 $\mu$ , the majority being from 10 to 18 $\mu$  in diameter. Most of the cells are round, and many have one good-sized round or oval nucleus that takes the stain well and is surrounded by a

variable amount of perinuclear protoplasm, the periphery of which is in many indistinct. Many of the nuclei are irregularly crescentic in shape and show deep constrictions. The nuclei that have not taken the stain deeply appear more or less granular and have from one to three nucleoli. The nucleus is centrally located in some of the cells, in others eccentrically. In a considerable number of cells the nuclei are multiple. The vascular supply is fair, the vessels having very thin and poorly defined walls. No evidence of encapsulation is found in any part of the sections.

*Diagnosis.* Round-celled (medium-sized) sarcoma.

FIG. 1.

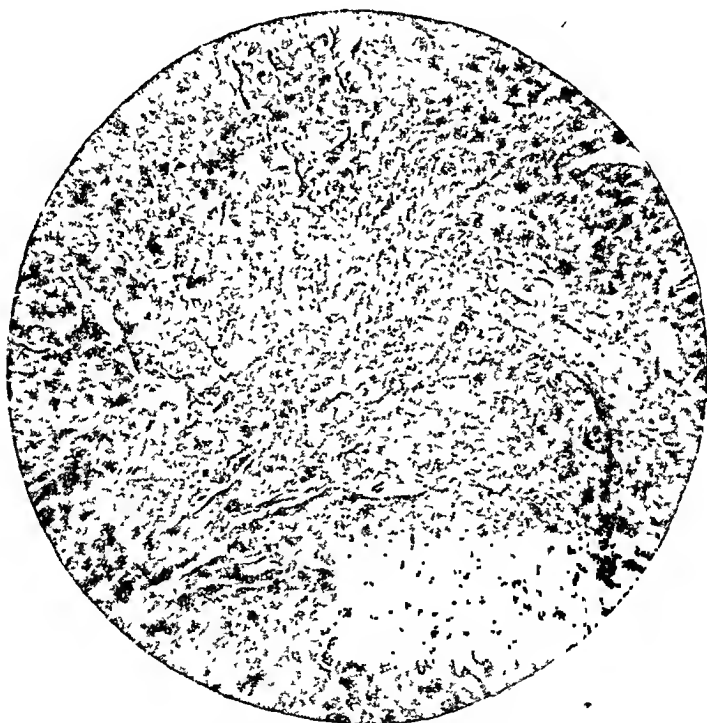


CASE I.—Round-celled (medium-sized) sarcoma of bladder.

CASE II.—J. T., aged fifty-three years, widower; bricklayer by occupation. Physique good. No history of malignant disease in family. Patient gives history of gonorrhœa seventeen years ago. Denies syphilis. Says that he has had more or less trouble in passing urine ever since he contracted the gonorrhœa. For the past four years he has had occasional attacks of hæmaturia, which are becoming more frequent. During the past year he has suffered very much also from painful and frequent micturition. He seems unable to empty his bladder, the stream often stopping suddenly, but beginning again after a change in position. At present the pain in the bladder is continuous, but much greater when he is urinating than at other times. He is obliged to pass urine from ten to fifteen times

during the day and oftener during the night. Has noticed blood in the urine at frequent intervals, also small masses that he thinks were blood clots. These masses block up the urethra when he is urinating, causing him great pain, which is partially relieved as soon as they are forced out by the urine. Catheterization has been necessary on several occasions recently. Bowel movements also cause him considerable pain in the region of the bladder. He is unable to work on account of the pain caused by moving the body. Thinks that he has lost some weight during the past year, but does not know how much. Appetite poor. The condition of the urine varies considerably at different times. Occasionally it is quite

FIG. 2.



CASE III.—Fibrosarcoma of bladder.

clear and free from sediment, but it usually has quite a heavy sediment consisting of pus and red corpuscles.

*Cystoscopic Examination.* The instrument was passed without trouble, no stricture being present. The bladder was found to be very much dilated. Occupying the base, involving the orifice of the left ureter and extending upward on the posterior wall three or four inches, is seen a large irregular mass having a cauliflower appearance. The growth is sessile and occupies a large part of the dilated bladder, being about three inches in height. Several pieces of the tumor were detached without trouble by the end of the cystoscope and sent in for pathological examination.

A week later a suprapubic cystotomy was performed and the growth thoroughly curetted. The operation was followed by cessation of all symptoms and when patient left the hospital three weeks later the bladder had contracted to nearly its normal size, and the mucosa appeared normal. He began taking x-ray treatment through the suprapubic opening, but died rather suddenly of uræmia seven weeks after being operated.

*Microscopic Examination.* Specimen consists of two pieces (2.5 x 1 x 0.05 cm. and 1.5 x 1 x 0.05 cm.), grayish-white in color. Hardened in increasing strengths of alcohol. Embedded in celloidin. One surface of the sections, presumably that projecting into the bladder, has a somewhat villous appearance; small projections of delicate connective tissue containing numerous small round and spindle-shaped cells extend outward, and are covered with from two to six or eight layers of cells measuring from 8 to 12 $\mu$  in diameter. These cells have large oval or round nuclei that take the stain deeply, and very little cytoplasm. The connective tissue contains a moderate number of thin-walled bloodvessels. Underneath this the connective tissue forms irregular alveoli in which the cellular material is compactly arranged. The deeper parts of the sections consist chiefly of cells with here and there a few fibres of connective tissue. The cells vary much in size and shape, measuring from 5 to 20 $\mu$  in diameter, some being round, some spheroidal, and some spindle-shaped. Bloodvessels are present in considerable number, and in most instances appear to be openings in the cellular material lined with endothelium. No suggestion of encapsulation can be seen.

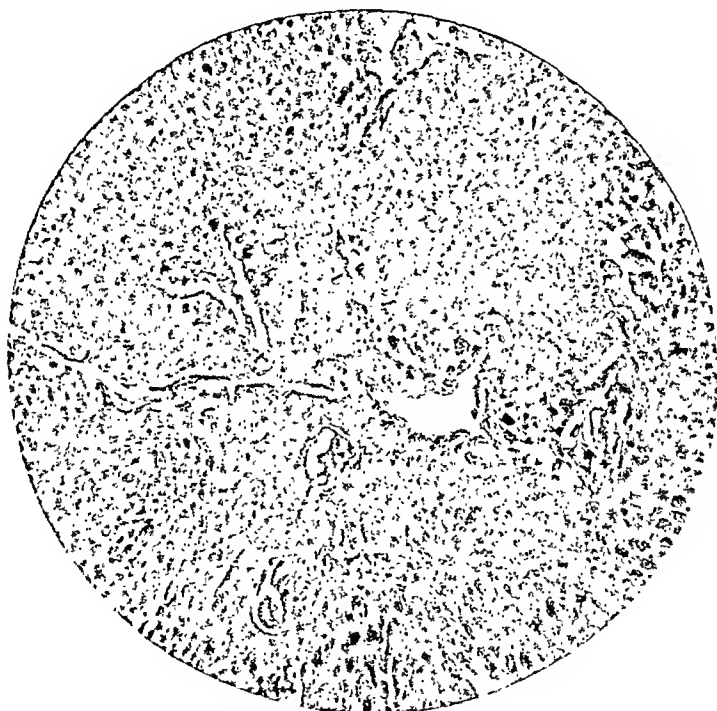
*Diagnosis.* Fibrosarcoma.

CASE III.—Male, aged sixty-two years; well preserved. No history of venereal disease. Six months ago had an attack of hæmaturia. This was soon followed by signs of vesical irritation. Has had several severe attacks of hæmaturia at irregular intervals since then. Has been troubled very much lately with strangury and frequent micturition, from which he has been unable to obtain relief. Has an almost constant desire to pass urine. For the past two months he has been getting up from twelve to fifteen times every night to urinate. Complains also of pains in end of penis, chiefly at end of urination, and a constant dull pain in "small of back." Any jolt or jarring of the body causes pain in the region of the bladder. Says that he has lost some in flesh, but does not know how much. On examination the prostate is found normal to the touch. The bladder appears to empty itself completely. The introduction of even a soft-rubber catheter into the bladder causes considerable bleeding. Urine 2400 c.c. in twenty-four hours. Pale in color; contains large amount of pus; some blood; no casts.

A suprapubic incision was made and a tumor one-half the size of a small orange was found, occupying the left half of the bladder

and apparently springing from the left lateral wall. Neither the ureteral nor the urethral orifices were involved. The growth was rough and nodular in appearance; it was rather soft and bled easily; did not appear to be ulcerated, and was pinkish in color. Pieces were easily removed for microscopic examination. No calculus was present. It was thought unwise to attempt the removal of the growth, so permanent drainage of the bladder was established. This treatment gave prompt relief from all the unpleasant symptoms, and the patient remained free from them for two months. At present, however, two and a half months after operation, all symptoms are recurring and the patient is rapidly failing.

FIG. 3.



CASE III.—Spindle and round-celled sarcoma of bladder.

*Microscopic Examination.* The tissue consists of three pieces ( $2 \times 1 \times 1.5$  cm.,  $1 \times 1 \times 1$  cm., and  $1.8 \times 2 \times 1.5$  cm. in size), and has a pinkish-white appearance. It was received in dilute alcohol and the hardening continued in increasing strengths of the same fluid and embedded in celloidin. The sections consist almost entirely of cellular material, an occasional strand of delicate fibrillar tissue being seen. The vascular supply is good, most of the blood channels being openings through the cellular material lined by a single layer of endothelium; some of the openings have no endothelial lining. A few small collections of leukocytes are seen scattered through the sections. The cells vary con-



siderably in size and shape, and contain nuclei that are round, spheroidal, and fusiform in appearance. The perinuclear protoplasm is scanty in amount and indistinct. Most of the nuclei take the stain deeply. The majority of the cells are mononuclear. The cells measure from 5 to  $15\mu$  in diameter, the majority being from 7 to  $10\mu$ . A few collections of small round and small spindle-shaped cells whose nuclei take the stain very intensely are seen. The connective tissue where present consists of delicate fibrils and small spindle cells very irregularly arranged. No evidence of encapsulation can be found in any part.

*Diagnosis.* Mixed-celled (spindle and round) sarcoma.

In looking over the statistics of these cases one is impressed by the frightful mortality and apparent hopelessness of the disease, only one case of the entire series, that of Stankiewicz,<sup>27</sup> being pronounced cured as late as *one year* after operation. In this case the diagnosis was made, let us emphasize, by means of the cystoscope, and the growth when removed was only as large as a small cherry. Although the clinical symptoms and other prominent features of the disease have already been summarized by previous writers (Southam,<sup>10</sup> Barling,<sup>3</sup> and others), I feel that it will perhaps be well to recapitulate and emphasize them here.

In studying these abstracts, including the three cases recorded in this paper, the following points may be observed:

1. That sarcoma of the bladder is most common after middle life (26 cases out of 50 occurring after the age of forty), and during childhood (14 cases out of 50 occurring under the age of ten), but that it may occur at any age.

2. It is more common in males than females (34 to 13).

3. The most constant symptom is hæmaturia. This symptom cannot, however, in many cases be considered an early sign, as the date of its appearance is probably significant in the majority of cases of beginning ulceration of the neoplasm.

4. Next to hæmaturia the most constant symptoms are those of cystitis and vesical irritation—*i. e.*, strangury; frequent and difficult micturition; small stream; retention; purulent urine.

5. Emaciation consecutive to the growth is present in advanced cases only.

6. A calculus may or may not be present.

7. In females the growth may invade the urethra and appear at the vaginal opening.

8. The disease is more rapidly fatal in children than in adults.

9. In those cases in which the diagnosis has been made early in the course of the disease, the neoplasm has been small, single, and apparently localized.

10. The growth may spring from the submucosa of any part of the bladder, but the most common location is at the base, in the vicinity of the ureteral orifices.

11. The growth is usually sessile, with a broad base; is usually soft and friable, more or less lobulated, in some cases has a cauliflower or villous appearance. The growths are usually single, but in the later stages may be multiple.

12. Metastases, as compared with sarcoma of other parts of the body, seem rare except in quite advanced cases.

13. The varieties of sarcoma occurring in the bladder so far recorded are round-celled (large, medium, small, lymphosarcoma, and alveolar), spindle-celled, mixed-celled, giant-celled, fibrosarcoma, myosarcoma, myxosarcoma, and chondrosarcoma.

14. At the present time our only hope for the cure of sarcoma of the bladder appears to lie in the early detection of the neoplasm by means of the cystoscope or by exploratory incision, and its complete removal at this stage of the disease.

NOTE.—Since this paper was completed and in the hands of the publishers my attention has been called to the report of a case of "Sarcoma of the Bladder and Prostate Gland Causing a Cyst of the Urachus and Bilateral Hydronephrosis in a Nine-months-old Baby," by Dr. G. McConnell (*Proceedings of the Pathological Society of Philadelphia*, April, 1904). Microscopic examination showed the growth to be a myxosarcoma.

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## A CASE OF SPONTANEOUS ARREST OF GROWTH IN AN ENDOTHELIOMA, WITH SUBSEQUENT INFLAMMATORY ABSORPTION.<sup>1</sup>

BY B. M. RANDOLPH, M.D.,  
OF PHILADELPHIA.

M. S., aged forty-three years, Hebrew, has always been healthy; four living healthy children; lost one in infancy; last child twelve years old. Symptoms pointing to beginning menopause are present.

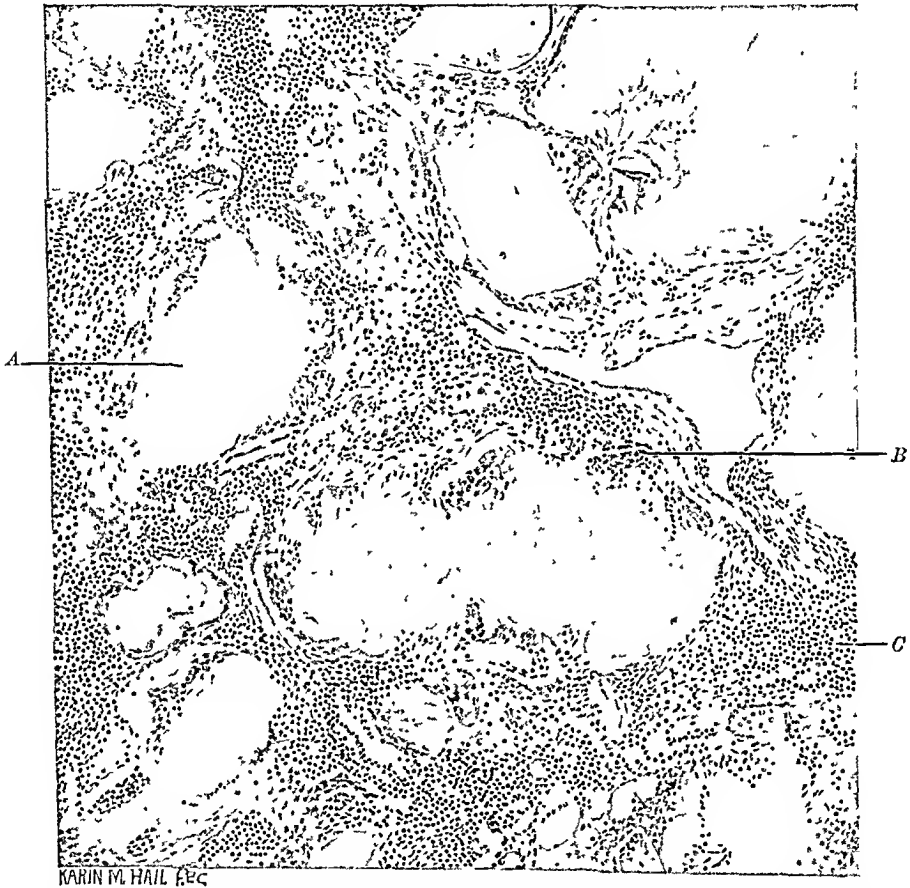
Three years ago there appeared on the posterior aspect of the left forearm, about the junction of the upper and middle thirds, a small nodule beneath the skin, which was movable and painless. In the beginning the patient squeezed and otherwise handled it, on one occasion bringing a little blood. The mass grew steadily and painlessly for six months, in that time attaining its present size. From that time till two weeks before operation it remained stationary.

<sup>1</sup> Presented before the Philadelphia Pathological Society, April 14, 1904.

Two weeks before applying for relief the mass began to be painful and to show signs of inflammatory reaction. The mass was excised by Dr. Steinbach at his clinic in the Polyclinic Hospital. Two weeks later the wound had healed by primary union. There was no evidence of recurrence six months after operation.

*Pathological Examination.* The mass is flattened, dense, has a smooth, glistening base. On the upper surface is a portion of normal

FIG. 1.



A. Alveolus containing necrotic cells. B. Giant cells. C. Round-celled proliferation in connective tissue. (Obj. 16 mm. Oc. 8  $\times$ . Formol-Muller. Hem.-eos.)

skin, which is not adherent nor in any way connected with the growth. The mass is flattened, slightly elliptical,  $1\frac{1}{2} \times 2 \times \frac{3}{4}$  inches. It has a capsule, which is derived from the surrounding connective tissue. On section it presents a grayish-white appearance composed of dry, friable, fibrous material.

Specimen fixed and hardened in Orth's fluid; sections cut with freezing microtome and stained with hæmatoxylin, hæmatoxylin and eosin, Van Gieson's stain, Unna's polychrome methylene blue,

Gram's stain, and Mallory's connective-tissue stain. The following appearances are found: The growth is surrounded with a thin connective-tissue envelope which is continuous with a connective-tissue stroma ramifying freely through the growth. This stroma is arranged so as to form alveoli of large size. These alveoli are filled with what appears under low power and high illumination to be a homogeneous degenerated substance, but which, under close examination, is seen to be made up of cells closely packed together, sometimes flattened so as to present a stratified appearance. These cell masses are clearly necrotic, as they do not take up nuclear stain,

FIG. 2.



KARIN A. HALL, fec.

A. Connective-tissue capsule. B. Healthy tumor cells. C. Area showing transition stage between healthy and necrotic cells. D. Cell necrosis complete. (Obj. 16 mm. Oc. 8 $\times$ . Formol-Müller. Hem.-eos.)

but are stained by eosin in the hæmatoxylin-eosin process and by picric acid in the Van Gieson method. Areas are observed where the necrotic process has not taken place. Here we see the alveolus is filled with medium-sized round cells, with round nuclei staining with moderate intensity. There can be no connective-tissue fibres demonstrated between the cells. The cell growth is evidently derived from the endothelium of the lymph spaces. That the above cellular necrosis affects such collections of cells as those just described is shown by the fact that the stages of transition from one to the other can be demonstrated. The connective-tissue stroma shows a very peculiar phenomenon. There is active hyperplasia,

with a very marked round-celled infiltration. New-formed blood-vessels are numerous. Very characteristic is the development of *giant cells*, which are very numerous and are uniformly applied to the margins of the necrotic cell areas, sometimes completely surrounding an alveolar space like a skirmish line. Their peripheral arrangement combined with the fact that they are so closely applied to the cell masses, and often adjust their shape to these masses (being long, slender, and flattened), make one believe that their function is phagocytic.

My opinion is that an endotheliomatous growth started in the subcutaneous connective tissue; that it grew steadily for six months, and then, for some unknown reason, became arrested; that a necrosis or atrophy of the cells of the tumor took place; that later this inactive tissue began to act as an irritant, and the response was a productive inflammatory process which endeavored to remove a foreign mass. The very abundant presence and peculiar arrangement of the giant cells seems to show that the function of these cells is an absorptive one.

I am aware that the belief that spontaneous healing of a malignant growth does not occur is so strongly rooted that it is the custom for pathologists to assume that such cases, when reported, are errors in diagnosis.

I present the evidence in this case without comment, allowing the history, the record of the examination, and the drawings made from the slides to furnish their own evidence.

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## THE MENTAL STATES ASSOCIATED WITH CHOREA.<sup>1</sup>

WITH A REPORT OF TWO CASES OF DEMENTIA CHOREICA.

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CHOREA has been known as a disease for centuries, and has popularly been so closely associated with the name of St. Vitus' dance since the Middle Ages that the original application of the latter term has been comparatively obscured. St. Vitus' dance was originally applied to the remarkable epidemic outbursts of combined mental and physical excitement which after the fourteenth century became known as tarantism or dancing mania. The sufferers resorted to the chapels of St. Vitus, in Swabia, Germany, for relief, believing the patron saint of these chapels to possess the power of curing them. Many neurologists, therefore, correctly

<sup>1</sup> Paper read before the California Northern District Medical Society, June 14, 1904.

confine the name St. Vitus' dance to the hysterical form, which has been termed chorea magna or major to distinguish it from chorea minor or true chorea.

In the light of the most recent investigations chorea has come to be looked upon as a symptom which may enter into the formation of different disease-pictures allied in their pathological nature.

Chorea has been defined as a frequent, more or less quick, irregular and involuntary clonic muscular movement of almost any part of the body, and is a symptom of a lesion or lesions of certain parts of the brain. Chorea has been observed in animals on which brain experiments had been performed, and it has preceded as well as followed hemiplegic attacks. It has been found in an epidemic form and combined with epilepsy and insanity, and is met with as a symptom in alcoholism and idiocy. It has been observed during pregnancy and following rheumatic fever. One form has been spoken of as the hysterical, another as the hereditary or chronic chorea.

Three forms of chorea are intimately associated with mental manifestations: the hysterical insanity of chorea magna, the delirium of chorea minor, and the dementia of the hereditary or chronic chorea.

1. Chorea magna, which is manifested by a succession of rhythmical movements of extension and flexion, is found more or less associated with disturbances of the various bodily functions which go to make up the stigmata of the general neurosis of hysteria, such as varying degrees of paralyses, hemianopia, aphonia, muscular spasms, distortions of head or body, globus, singultus, fainting spells, etc., which symptoms, as well as mental manifestations, characterize the disease-picture of hysterical insanity. The mental disturbances vary greatly in character. Sometimes a motiveless melancholy or anxious depression seizes the patient, in which ideas of guilt and persecution are mingled with visions and hallucinations of an insulting nature. At other times we see conditions of excitement, usually in the form of irritability, with violent spells of cursing and tendency to destroy or to smear, the excitement being generally associated with some external cause, such as worry, jealousy, etc. These conditions are, as a rule, of short duration—hours, days, or weeks—but with a marked and irregular tendency to relapses. The most characteristic of the psychic disturbances met with in hysterical insanity are, however, the dream states (*Dämmer-zustände*), which are attacks of shorter or longer duration in which consciousness becomes clouded to a marked degree, the attacks occurring alone or in immediate connection with convulsions, which may sometimes terminate or interrupt the attacks.

2. The true form of chorea, chorea minor or Sydenham's chorea, first accurately described by Sydenham in 1688, is a disease in which the choreic movements completely control the disease-picture

the muscular movements being at all times more or less influenced by excitement. The patient is self-conscious, embarrassed, for which reason Prof. Christian Gram,<sup>1</sup> of Copenhagen, has called it *morbus trepidationis*, as compared with Basedow's disease, which might be called *morbus timoris*. The cause of this disturbance is undoubtedly an infection which is probably similar in nature to that of acute articular rheumatism. Wasserman and Westphal were able to isolate a streptococcus from the brain of a choreic, the pure culture of which produced in turn articular rheumatism in the rabbit. It is, moreover, a fact that in cases of choreic delirium one may almost always find an association with endocardial or rheumatic disease.

That individuals suffering from chorea vera are mentally affected is a well-known observation, though the degree of mental implication is usually not grave. It is seldom that this influence amounts to more than a condition of more or less marked fatuity—rarely a real psychosis. The character of the child affected becomes changed; there are lapses in the moral sense, mendacity, perverseness, emotional outbursts, and irritability. Disturbances of memory and of the faculty of attention are also common. The child loses what it has previously learned. Among children, Dr. Friis<sup>2</sup> could not find a single instance where the mental implication amounted to a real insanity. Among ninety-three cases of chorea he found thirty-four cases in individuals over fifteen years of age, and among these he had seen seven cases in which the mental symptoms developed into a real delirium or psychosis. Kraepelin<sup>3</sup> describes the psychosis met with in such cases as follows:

"We find a dream-like confusion and mental dulness with peculiar incoherency of thought and some hallucinations and delusions, an irritability of mood, and the characteristic choreic movements. The patients, as a rule, receive impressions from without in a fairly normal manner, but they are very inattentive, easily diverted, quite unable to express themselves coherently, incognizant of their own circumstances or surroundings, give expression to monotonous, abrupt sentences into which they at times weave chance observations. They hear their relatives call, perhaps perceive imaginary beings, fear that they are to be killed or poisoned; but all that they experience is vague and without elaboration. The mood is sometimes anxious, sometimes childishly jolly, varies greatly, and sometimes leads to violent fits of anger. The whole disease-picture is dominated by the very severe choreic restlessness which, with short interruptions, continues day and night, and which may even to a considerable extent endanger life. The patients jerk, flounder

<sup>1</sup> Chorea infectiva (Sydenham's chorea) og dens Behandling, Hospitalstidende, January 17, 1900.

<sup>2</sup> Om chorea hos Voksne, Hospitalstidende, June 29, 1892.

<sup>3</sup> Psychiatrie, Bd. ii., Siebente Auflage, 1904, p. 22.



about, pitch and twist the arms, bore the head into the pillow, strike themselves indiscriminately, make faces, shoot out the tongue, gasp, smack the lips, toss themselves about. Sleep is almost entirely absent; the taking of nourishment is made very difficult. This excitement fortunately does not, as a rule, remain at its height for more than a few days or weeks, after which it gradually subsides. Consciousness and rationality return, hallucinations and delusions disappear, the much diminished body weight makes a quick increase. The patients, however, remain for some time irritable, easily fatigued, and show a tendency to noticeable changeability of mood."

These mental manifestations, at times complicating Sydenham's chorea, are quite different from those found associated with the chorea of hysterical insanity or with Huntingdon's chorea. In the former they are characteristic of the hysterical dream state, which takes a quick but much less serious course, and is mentally more easily influenced; in the latter, the accompanying mental manifestations have the stamp of a progressive dementia.

3. The hereditary form of chorea has been called Huntingdon's chorea,<sup>1</sup> Dr. Huntingdon having supposedly first described the disease in 1872. The disease was, however, first spoken of by Dr. Waters in 1841, who found it not uncommon in certain parts of the State of New York. The first case observed in Europe was described by Landouzy in 1873; the next two cases were reported by Ewald in 1884. From this year until 1892 a couple of dozen cases could be collected from the literature. It has not been generally thought to have a well-founded relation to Sydenham's chorea, although it was considered identical with it by many French neurologists. The hereditary form has been more frequently met with in the State of New York than in any other part of the United States. Huntingdon found it only on Long Island, where chorea vera is comparatively rarely met with. It has been observed among the lower classes of society in other parts of America, and especially in families with many children. The disease has been variously denominated Huntingdon's chorea, chorea of the aged, family chorea, adult hereditary chorea, chronic chorea, and chronic progressive chorea. Dr. Huntingdon<sup>2</sup> found it present in a number of families living in the southeastern part of New York, and it was locally known as "the megrims" or "megrums," and, owing to their peculiar difficulties in walking, the patients were commonly called "shakers." The disease has a marked hereditary character which is peculiar in that it appears at an earlier age with each succeeding generation. It has been traced through five generations, and is said never to reappear once the hereditary chain is broken. It has been described as being to such an extent hereditary in some

<sup>1</sup> Spelled incorrectly by most writers Huntington's chorea.

<sup>2</sup> Archibald Church. *Nervous Diseases*, 1899.

families that in certain districts marriage<sup>1</sup> was prohibited within the affected families. Dr. Diller gives an example of its hereditary tendency in a family in which during four generations thirty-four cases developed, and ten of the cases during the fourth generation showed themselves even before the twenty-fifth year, in one case as early as the eighth year. The disorder has an insidious onset in adult life, and it affects the male sex in greater proportion, in this differing from chorea vera. It usually appears at the age of from thirty to forty-five years, but may develop at any period, as early as eight years and as late as sixty. While the choreic movements develop slowly and gradually, they seem at first under the influence of the will, and entirely absent during sleep. As a rule, they show themselves at first in the lower extremities, and are not preceded by rheumatism, heart affections, paralysis, or muscular atrophy.

Kraepelin places Huntingdon's chorea in a group of gradually progressing mental disturbances with the diseases known as diffuse cerebral sclerosis, gliosis of the cerebral cortex, multiple sclerosis, etc. The mental symptoms of the disease are excellently described by Kraepelin<sup>2</sup> in his text-book as follows:

"The patients become forgetful, weak in judgment, lacking in depth of thought, seclusive, dull in mood, but irritable and wavering. They become incapable of regular activity, and not infrequently make attempts at suicide or other violent acts. A patient whom I had under observation strangled his three little children, whom he thought he could no longer support, after which deed he quietly took a walk and remained quite indifferent as to his criminal act during the legal progress of the case.

"Now and then sensory hallucinations or persecutory ideas are detected which are related by the patient without special emphasis. At times conditions of fear, violent outbursts of temper, or tearfully elated behavior are met with. Among physical manifestations the most striking are grimacing and the peculiar recurrent, jerky or swaying movements of the head, trunk, and limbs, which differ from those of chorea vera by their lesser severity and extent; they usually become increased by mental excitement. The speech is hesitating, at times indistinct, blurred; the handwriting is somewhat irregular. The movements are unsteady, the gait is reeling, standing with closed eyes is rendered difficult, the sprawling fingers tremble. The general physical strength does not, however, appear to have suffered any appreciable diminution. The tendon reflexes and the mechanical muscular irritability are increased. The pupillary reaction remains intact; sensibility does not show any disturbance. At times one meets with very intense headaches. Epileptic or apoplectic attacks occur in a few cases.

<sup>1</sup> Reynolds. *Medical Chronicle*, April, 1892.

<sup>2</sup> *Psychiatrie*, Bd. ii., Siebente Auflage, 1904, p. 402.

"The disease makes an uninterrupted but slow progress, covering a period of ten to twenty years, toward a pronounced dementia, which, however, does not reach the high degree found in cases of paresis. There likewise appear to be certain limits to the degree of severity of the physical symptoms; the chorea may even subside until light traces only can be detected. The disease-picture is principally differentiated from that of general paralysis, with which it may to a certain extent be confounded, by the clinical peculiarities as well as by the absence of pupillary disturbances, the characteristic defects in speech and handwriting, the paralytic symptoms, and especially by the accompanying chorea. The form of the dementia, which, while it does not to such an extent lead to defect of memory and incognizance of time in this disease as in general paralysis, does from the start tend to annihilate to an equal or greater extent the mental and emotional activity, likewise enables one at times to make the differentiation.

"The post-mortem findings show chronic meningitic changes, thickening and small-celled infiltration of the pia as well as atrophy of the brain, atrophy of the fibres, probably also degeneration of cortical nerve cells, diffuse changes in the vessels with dilatation of the perivascular spaces and proliferation of the adventitia. Remnants of old hemorrhages are found in the neighborhood of the vessels. In a case observed by me Nissl was able to demonstrate chronic cell changes, glia-proliferation, and hypertrophy of the pia, but he did not find either noticeable vascular disease, atrophy of fibres, or cortical atrophy. The spinal cord appears to be involved in the pathological process, although to a very variable extent."

The following two cases of Huntingdon's chorea have been under my observation during the past one and one-half and two and one-half years:

CASE I.—N. N., native of New York, aged sixty-five years, divorced, has five living children and one dead, admitted to Stockton State Asylum, November 8, 1901. He has lived forty years in California, is a miner by occupation, and has led a lonely life in the mountains for a number of years prior to admission. It is stated in the commitment paper that he is given to prowling around at all hours of the night, that he gets excited if remonstrated with, and is uncontrollable. He talks irrationally, refuses to eat what anyone but he himself cooks, for fear of being poisoned. Uncontrollable, spasmodic muscular movements in the extremities, trunk, neck, and face are present, which cause him to spill food on himself when he eats, and he is generally filthy in his habits. He has frequently been heard talking to himself when alone in his cabin, and is quite irritable in disposition; no one of his children has any influence over him. He cannot take care of himself, and will not allow others to care for him. He roams about annoying his neigh-

bors and frightening women. According to information obtained from one of his sons, he was first observed to make choreic movements at the age of forty-eight years. These movements were slight until he had a severe attack of la grippe, when about fifty-seven years old. After this they became more and more severe, and he seemed more irritable and seclusive. The patient's father suffered from a similar complaint, choreic movements, which came on after he was some fifty years old, and continued until his death, at the age of about eighty. The mother of the patient died of tuberculosis. Nothing is known about his paternal relatives. The patient's father had six sons, one by a second marriage, who died at the age of ten, and who, during the last two years of his life, also presented symptoms of chorea. The five living children of the patient are all well; none of them have up to this time been afflicted with chorea.

The patient, upon examination, is found incognizant of time and place; talks jerkily and with difficulty on account of violent choreic movements of the tongue, lips, and facial muscles. He is restless during the day, wandering about the ward aimlessly. The involuntary clonic muscular movements are present in all four extremities, though more marked in the arms than in the legs. While they vary greatly as to severity, being more marked when he is spoken to or excited, they at all times affect one part or another of the body, including the muscles of the trunk, shoulders, neck, and face. Now and then jerky sighs or spasmodic inhalations are observed, showing involvement of the diaphragm. The patient is entirely free from involuntary muscular movements when asleep, and the exercise of will power diminishes the jerking to some extent. There are no motor or sensory paralytic symptoms present, nor any marked diminution in muscular power. The knee-jerks are apparently absent or nearly so, even with Jendrassik. No paralysis of sphincters. Mechanical muscular irritability not markedly increased; no nystagmus; some blepharospasm. Tension and pupillary reaction normal.

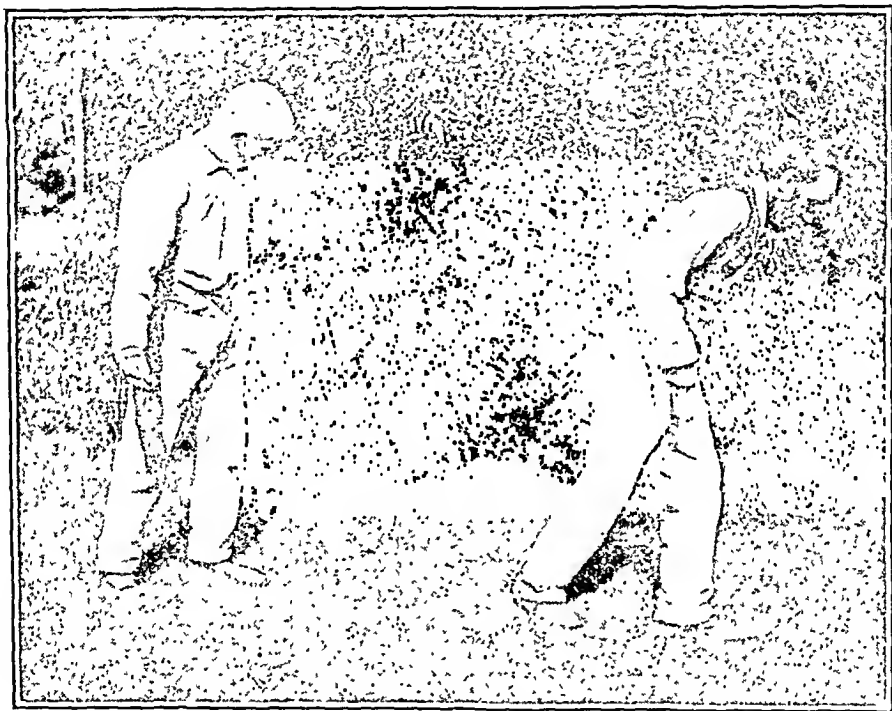
The patient was confused as to surroundings and filthy in his habits (a feces-smearer) when first admitted, but after some months improved in this respect. Since then there has been a slow but gradual increase in the feeble-mindedness. He is duller mentally, shows loss of memory, taking little interest in surroundings, and comprehending little of what is said to him. The choreic movements have not abated in severity, and involve as many parts of the body as when first examined, over two and one-half years ago. His speech has become an almost unintelligible babble.

CASE II.—I. F. I., native of Indiana, was admitted to the asylum February 11, 1903, when forty-five years of age, and after having been in California eighteen years. He is single, blacksmith by occupation, not addicted to liquor to excess. He has been an inmate of

the County Hospital for some time, and has of late become restless, irritable, and quarrelsome, and shortly before his commitment made an unprovoked violent attack upon the steward of the hospital. The commitment paper gives one but little information about the patient, but a sister says that the choreic movements which are present date back a little over eleven years and set in shortly after an accident. He was thrown during a runaway, landing on his head, and remained unconscious for a number of hours. After he had recovered consciousness at a hospital, to which he had been taken, it is stated that he was unable to move for some days, and that he had lost all sensation in his left side, "which felt like a dead person to his right hand." After some months the sensation in his left side returned, and has been about normal since that time. It is stated that about a month or so after the accident he was seen to make the involuntary clonic muscular movements, which at first were slight and bilateral, but have gradually been growing more and more marked during the past ten years. For some years he would only stagger as if he had made a misstep. The sister is quite sure that he had no jerking before the accident. His mother is said to have been insane, and a maternal aunt likewise. His father died of apoplexy. There is no history of any case of chorea either on the paternal or maternal side. His father had three children, besides himself, by his first wife, and three by a second wife, but none of these children developed symptoms of chorea. Upon examination at the insane asylum he is found cognizant of surroundings but confused as to time. His memory is poor; he is often observed to talk to himself, is slow of comprehension, and it is difficult for him to make himself understood on account of the choreic movements about the tongue and lips. The involuntary clonic spasms are present in all four extremities, especially in the arms. The muscles of both sides of the face are implicated—the frontal portion of the fronto-occipital, corrugator supercilii, occasionally the muscles about the angles of the mouth, lower lip, and jaw. It is difficult for him to put his hat on his head. When told to hold his hands steady they jerk less. He totters and wiggles less with closed eyes. The shoulders are frequently lifted. When in bed and awake he twists about considerably, but is perfectly motionless when asleep. When told to put out his tongue he shoots it out for an instant only, and keeps up this play with the tongue as long as he endeavors to keep it outside the mouth. There is no motor or sensory paralysis. The knee-jerks are about equal and slightly increased. The pupils react to light; tension is normal; there is no nystagmus, but a slight blepharospasm. The examination of the fundus, kindly made by Dr. B. J. Powell, of Stockton, showed a congested retina and slight atrophic spots on the inner side of each disk, together with a Fuchs coloboma to a slight extent. (The retina and optic disks were found normal in the first patient, N. N.). When the

patient walks he turns about and glides along like a person learning to skate on the ice, the body bent forward as in paralysis agitans, and one shoulder drooping, often leaning to one side. His left foot frequently turns outward, the right one inward. He has a voracious appetite; thirst normal. Urine normal.

A depression is found on the head in the median line and about four inches above the occipital protuberance. It is saddle-shaped, does not appear to extend to the inner table of the skull, and measures about one inch transversely and half an inch longitudinally. A cicatrix is found about the centre of the depression.



Paralysis agitans-like attitude and propulsion in Huntington's chorea.

During the past eighteen months there has been no observable change in the choreic movements. The feeble-mindedness is a little more marked.

The above cases, when observed side by side, are perfect copies one of the other as far as the muscular movements are concerned. When walking they show a striking resemblance in posture to the propulsion seen in cases of paralysis agitans, as in the accompanying illustration. The large and small spasms are mixed in kaleidoscopic fashion, and there is likewise a marked difference in their velocity. Sometimes they are very quick, extending over a large group of muscles, at other times they involve but few muscles about the trunk, face, or fingers. Although the sprawling flexion and extension of the fingers are now and then observed

as in athetosis, the slower, rhythmic motion described as characteristic of athetosis is not present. There is, in fact, no rhythm about the spasms; the muscular activity is started now here, now there, and usually in several parts at the same time, reminding one of the antics of a jumping-jack.

There is a very close relationship of Huntingdon's chorea to athetosis; they appear to differ only in the velocity and homogeneity of the movements. Some writers, among others Strümpell, have even described a congenital athetosis with the muscular movements observed about the head, trunk, and extremities.

It is rather remarkable that the first case, which shows the family heredity, which Huntingdon had met with in New York, should hail from that State. The father and half-brother were found to have been subject to the disease. Beyond the father, the history of the family could not be traced.

The second case would seem to be of traumatic origin. The history of the trauma and of the symptoms immediately following it is incomplete, but it would seem to show that the paralysis following the trauma was confined to a sensory paralysis of the left side, which lasted some months. There is no history of a hemiplegia and no history that the choreic movements were unilateral at their onset; on the contrary, the sister says positively that when first noticed they affected both sides of the body. There is, as stated above, no observable difference in the velocity of the muscular movements in the two cases, and the mental symptoms are about the same in each case. The second case is more subject to emotional outbursts, but in each case we find the irritability, seclusiveness, history of persecutory ideas, characteristic speech defects, and progressively increasing dementia.

A traumatic origin of Huntingdon's chorea is spoken of by Westphal,<sup>1</sup> who reported a case in which the chorea developed soon after a fall from the third story, the patient being injured about the head, but sustaining no fracture of the skull. There was no hereditary neuropathy in the case. The terminal state of Huntingdon's chorea being so characteristic, there is good reason for the name, dementia choreica, as suggested by Hallock.<sup>2</sup>

With regard to the pathogenesis of chorea and choreiform conditions, chorea minor was spoken of by Prof. Christian Gram at a recent congress on internal medicine at Copenhagen as an infectious disease which develops after the infection has passed, like the post-diphtheritic paralysis. The opinion was expressed that the other forms of chorea, which are more or less of a chronic nature, such as Huntingdon's chorea, Unverricht's myoclonia, hysterical chorea, electric chorea, etc., have many points in common with

<sup>1</sup> Ueber Chorea chronica progressiva, Deutsche med. Wochenschrift, No. 4.

<sup>2</sup> Journal of Nervous and Mental Disease, 1898, No. 12.

hysteria and epilepsy, and probably have a kindred pathology in the cortex.

Dr. Lundborg, of Upsala, has expressed the view that these diseases may be connected with perverted metabolism of the ductless glands, which Ohlmacher holds is true of epilepsy.

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## A REPORT OF TWO HUNDRED AND EIGHTY-ONE MASTOID OPERATIONS, WITH SUBSEQUENT RESULTS.<sup>1</sup>

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THIS report is made from the data collected from 281 consecutive mastoid operations performed at the New York Eye and Ear Infirmary during the year ended December 31, 1903.

One hundred and fifty-six operative cases were personally followed up until the result in each case was known. The collected notes are herewith reported in the hope that they may prove of some value to those interested in mastoid surgery.

**AGE.** Of the total number of hospital patients admitted with acute or chronic otitis media, 447, about one-fifth were children; nineteen were babies under one year of age.

**MICROSCOPIC EXAMINATION.** To determine the infection cover-slip smears for microscopic examination were made from the aural pus before operation when possible; and, in many cases during the operation, from the pus found in the mastoid.

In the canal discharge diplococci and "latent"<sup>2</sup> streptococci were found in 49 cases; streptococci in 38 cases; pneumococci in 37 cases; and a mixed infection in 43 cases. Influenza bacilli were found in only 2 cases, and in 2 cases the spirillum of Vincent was found.

Of the 69 cases where the mastoid pus was examined streptococci were found in 50 per cent. and pneumococci in 29 per cent. In considering the prognosis of any acute case due weight was given to the presence of the streptococcus in the canal discharge; the pneumococcus infection was less violent.

**PHYSICAL EXAMINATION.** Mastoid swelling was found in 100 out of 447 cases. In 72 of the 100 cases, pus, subperiosteal, was found on operating. In the remaining 28 cases the swelling proved

<sup>1</sup> For the permission to make this report I am indebted to the visiting surgeons, Drs. Gorham Bacon, Adams, Dench, Whiting, McKernon, and Lewis, in whose service these cases occurred.

<sup>2</sup> Dr. George S. Dixon, the Pathologist of the Infirmary, who made the bacteriological examinations, informed me that in many cases where diplococci alone appeared in the smear from the aural discharge, cultures from the pus showed the streptococcus pyogenes. Subsequent operation often revealed pure streptococci in the mastoid pus. He, therefore, designated such diplococci "latent streptococci."



to be œdema, likely the early stage of subperiosteal abscess, as pus within the mastoid process was found.

Of the 72 cases of subperiosteal abscess 56 were in children. Only 16 were adults, showing the relative infrequency in adults of a perforation of the outer table of the mastoid with resulting subperiosteal abscess. In children the mastoid swelling appeared, as a rule, as one of the earliest signs of mastoiditis and was frequently the first sign indicating to the mother that the ear was the cause of the child's sickness. On the contrary, in adults mastoid swelling proved a late symptom, the histories of the acute cases varying from several weeks to four months.

**MASTOID TENDERNESS.** In most of the acute cases the tenderness was most marked over the antrum and at the tip, with moderate tenderness over the whole mastoid. In 84 cases the tenderness was fairly well confined to the two locations; in 3 cases the tenderness was solely over the antrum.

In 8 cases the tenderness was solely at the tip. In 2 cases where acute tip tenderness was present, operation revealed pus under the tip in the digastric fossa, the result of the extensive mastoiditis with perforation of the inner table at the tip, constituting a Bezold perforation. In several other cases moderate tip tenderness proved an unreliable sign, in that pus was found elsewhere in the mastoid. In 1 case, a radical for necrosis of the middle ear with history of otorrhœa, mastoid pain, and recent tip tenderness, a sclerotic mastoid and no pus was found on operation.

Marked post tip tenderness was present in 14 cases, nearly always associated with antrum and tip tenderness, and usually meant extensive involvement of the mastoid.

It might here be mentioned that in 2 cases seeking treatment for mastoid tenderness and swelling, examination revealed erysipelas, independent of any ear trouble.

Thirty-seven of the 281 cases seeking operation presented post-auricular fistulæ. Seven were the result of subperiosteal abscesses that had ruptured with subsequent discharge through the opening.

Thirty fistulæ were the result of former mastoid operations that were not successful. (Fifteen operated on at the infirmary required re-operation.) Of the 30 all but 7 were children, an unusually large proportion of failures in children from the mastoid operation.

There were also 7 cases, previously operated on, in which an abscess in each case developed under the old scar. In 4 cases, although the mastoid had healed well, the otorrhœa had continued in 1 case for one year, in others for three years, and in the 4th case for eight years before the mastoid abscess again formed. These indicate plainly that a mastoid operation for an *acute* ear should not be regarded as successful, even if the mastoid wound heals, unless the acute middle ear suppuration ceases, and the middle ear regains its normal condition. No case of true recurrent mas-

toiditis after operation came under personal observation in this series.

**MEMBRANA TYMPANI.** The usual appearances of the drum membrane in the acute cases were those commonly observed, namely, a beefy red bulging membrane, with or without a perforation, accompanied frequently with more or less sagging of the posterosuperior canal wall at its juncture with Shrapnell's membrane.

There were two rare cases of mastoiditis in which the drum membrane varied slightly, if at all, from the normal in appearance. The examination notes in one case are worth reporting in full, as follows: Two months ago stuffiness, deafness, and pains began in the right ear; after two weeks pain in and behind the ear became severe, unable to sleep; leeches applied and membrana tympani incised by family physician. Claims that there has been no aural discharge at any time.

*Examination.* Mastoid, œdematous, tender, acutely over antrum and tip; meatus, normal; membrana tympani not inflamed and of pearly pink color; manubrium distinct; slight bulging and injection of the periphery. Hearing fair, watch three inches, whisper and speech good in right ear. Operation revealed pus throughout the mastoid cells; the sinus groove was uncovered, exposing the lateral sinus at the knee. The sinus wall was here covered with granulations. Subsequent result. Recovery, mastoid healed with good scar; membrana tympani normal and with good lustre. Hearing normal.

The second case was a child with a subperiosteal abscess, with clear history of ten days' duration of ear trouble, during which no discharge was noticed by the mother. Examination showed that the drum membrane was not inflamed and not perforated; there was slight bulging, but not enough to completely obscure the manubrium. Operation revealed a subperiosteal abscess and pus within the mastoid. Recovery.

These two cases are reported at some length as they go to show that there are undoubtedly rare cases where suppurative inflammation of the mastoid may exist when the drum membrane may be slightly, if at all, inflamed. It is of course probable that the drum membrane and the middle ear cavity may have been inflamed at the onset, at which time an examination would have revealed the usual appearance of such inflammation.

**FEVER AS A SYMPTOM OF ACUTE MASTOIDITIS.** On admission 8 cases had normal temperature; in 93 cases the temperature was below 100°; in 54 cases, between 100° and 102°; in only 13 cases was the temperature between 102° and 104°; and in only 1 case over 104°, that a baby of three months who had meningitis on admission to the hospital. Thus in over one-half of the cases there was very little fever (under 100), and in only thirteen of the cases did the fever exceed 102° on admission to the hospital,

**ABORTIVE TREATMENT.** Of the 167 acute cases that did not come to operation, and were treated by paracentesis and irrigation, with ice-coil or leeches to the mastoid, six returned after their discharge from the hospital. One of the six cases was advised and refused operation, and left the hospital after six days' treatment to return later for operation. The remaining five cases show the delusive effects of the ice-coil to the mastoid. In all five cases the mastoid pain and nearly all tenderness disappeared, though there was no marked change in the quantity and character of the discharge under the ice-coil. One left the hospital on the second day, one on the third, one on the sixth, and two on the seventh day. The last two were, however, warned against, but insisted on leaving the hospital, supposing they were well. All returned with marked mastoid pain and tenderness. Four were promptly operated on and one case begged for delay. The ice-coil was again used in this case with the same result as before, namely, pain and tenderness disappeared though the discharge continued. The patient again left the hospital feeling well, and returned for the second time two weeks later for operation. Operation revealed in all six cases of extensive mastoid destruction, and in five of the six cases necrosis of the inner tables and consequent inflammation of the sinus or dura. (It is worth noting that all the six cases were adults with the outer table of the mastoid hard and thick.) In one case the perisinuous abscess was quite large, at least 2 c.c. of pus, and in another a Bezold perforation had also taken place. Fortunately thrombosis had not taken place in any of the 6 cases and recovery was uneventful.

The rule generally followed in acute cases, and considered safe by those who advocated the use of the ice-coil (and some did not), was to use the ice-coil during the first two or three days only, after the onset of the mastoid symptoms, and never at all in mastoiditis following a chronic ear; the coil to be removed at the end of thirty-six hours and not reapplied.

**OPERATIONS.** Of the 281 operations, 164 were mastoids for acute mastoiditis following acute suppurative otitis media. Forty-four were radical operations performed for mastoiditis following chronic suppurative otitis media. Twenty-five were radical operations secondary to former mastoid operations that had not proved successful—*i. e.*, a post-auricular sinus and otorrhœa had persisted; and 48 were radical operations performed primarily for the purpose of curing a chronic ear, where no symptoms of pus in the mastoid existed. (It is noteworthy that there were but three ossiclec-tomies performed during the year's service.)

Notes on the cases were made each day following the operations, and subsequent notes were made embracing the condition on discharge from the hospital, and the subsequent condition, including, where possible, hearing tests.

**MASTOID FINDINGS.** Pus was found, subperiosteal, in 72 cases, 53 of which were acute cases. Pus throughout the mastoid cells and none subperiosteal was found in 82 cases. Pus confined to the tip cells and none elsewhere, except in the antrum, was found in 24 cases. Pus solely in the antrum, with granulations and mucoid-like substance throughout the mastoid cells, was found in 27 cases. Smears, made in a few of such cases from the cell contents, showed pus organisms.

In 2 of the 164 cases operated on for acute mastoid symptoms the mastoid cells were found apparently normal, except for some congestion.

Cholesteatoma was found in 20 chronic cases.

**SCLEROSIS.** The mastoid process was completely sclerotic, except the antrum, in 28 cases, all in chronic ears. In no one of the 281 cases was the antrum wanting, although in most of the sclerotic mastoids the antrum was small, and in one case it was a mere enlargement of the posterior end of the aditus, and was found with difficulty. It is worth noting that the lateral sinus lay far forward as a rule in all of the sclerotic mastoids, and was accidentally opened by reason of its abnormal position in 2 cases. Only care in chiselling prevented its being opened more often. In 2 sclerotic mastoids the sinus was exposed on chiselling through the suprameatal triangle, usually considered a safe landmark for opening the antrum, and it was necessary therefore to reach the antrum after the Stacke method by chiselling through the external attic wall and working backward to the antrum. In one of these cases, after the initial incision and retraction of the periosteum, the sinus showed through the thin cortex immediately below the suprameatal triangle. Its bony covering was of the thinness of a small visiting card.

Also, in the sclerotic mastoids, the histories show periodic attacks of mastoid pain without much or any tenderness. In 9 chronic cases operation was sought in each case largely on account of the pains, rather than on account of the danger from chronic suppuration of the middle ear. The pains were, as a rule, relieved after operation.

The dura was uncovered and found normal in 44 mastoids and 45 radical operations. In 2 cases, both babies with subperiosteal abscesses, meningitis subsequently developed and death followed. In all the other cases no harm resulted, which accords with previous observations of the great resisting property of the dura. In no case was the dura accidentally opened.

Epidural abscesses were found in 21 cases, 12 mastoids and 9 radicals. Meningitis, followed by death, occurred in 2 cases, both adults, with extensive mastoid involvement. One had been advised but refused operation two weeks before.

In one case the symptoms by no means indicated the extent of the dura involvement. The history showed constant otorrhœa

for five years until one week ago, when the discharge ceased and the pain began. There was scant mastoid tenderness and slight fever that subsided in a few days. After five days' hospital treatment a radical operation was determined upon, largely because of the certain middle ear necrosis. A large perisinuous abscess from the knee downward was found. The surrounding dura was covered with thick yellow exudate to the extent of 1 x 2 inches. Result, recovery.

The lateral sinus was uncovered intentionally, or unintentionally, and found normal during 69 operations. In no case did harm result from the exposure. The sinus was accidentally opened in 9 of the 281 operations. In 8 cases no harm resulted. In 1 case sinus thrombosis followed. The notes in this case are as follows:

P. R., aged eighteen years, admitted with history of constant otorrhœa for three years. Two weeks ago the discharge ceased, and headache and dizziness began. Examination shows mastoid œdema and tenderness. Operation revealed thick yellow pus on chiselling through the hard cortex. The antrum was full of foul-smelling cholesteatoma. The bony wall of the sinus was necrotic and the sinus covered with lymph and granulations in its descending portion. The sinus was accidentally opened while further uncovering the diseased area. Free hemorrhage resulted, was easily controlled and the operation proceeded. After operation the subsequent history was uneventful until the eleventh day when patient had a slight chill, temperature going to 105°. No vomiting or headache, no optic neuritis, and no jugular sigus. The mastoid wound was clean with healthy red granulations. However, on account of the irregular temperature during the next three days, a second operation was performed. The sinus was exposed and found thrombosed; the thrombus removed, with free bleeding from above, but none from below, showing that the thrombus extended down into the jugular. The neck was then opened; the jugular vein found collapsed above the union of the facial vein; was ligated and excised as high up in the neck as possible. Some emboli from the septic thrombus had, however, already entered the general circulation, for three days later a cough and pain in the chest began, ushering in septic pneumonia, in patches in both lungs, which after seventeen days of irregular fever, sweats, foul expectorations and progressive exhaustion, caused death.

In the remaining 8 cases of accidental opening of the sinus no harm resulted. The gauze pledgets over the site of injury were not removed as a rule for four or six days. In one case removal of the pledget on the third day resulted in free bleeding requiring painfully tight packing. At the second dressing bleeding again occurred, and was similarly controlled and did not subsequently recur.

The lateral sinus was purposely opened, because of suspected thrombosis in 11 cases, in 9 of which thrombosis was found. In

the other 2 cases the sinus looked suspicious of thrombosis, and was incised to determine definitely its condition. No clot was found in either case; free bleeding occurred; both cases made good and uneventful recoveries.

**SINUS THROMBOSIS.** Of the 9 cases of sinus thrombosis 7 resulted from extensive mastoiditis following chronic middle ear suppuration, and only 2 from an acute middle ear suppuration. This is in accord with the reports of other observers, and emphasizes the danger from a chronic ear. In 3 cases of thrombosis the prognosis on admission was bad. The symptoms in 2 cases indicated that the thrombus was undergoing septic disintegration, with the probability that septic emboli had already entered the general circulation. The notes of these two cases are as follows:

A. S., aged eighteen years, admitted with history of otorrhœa since childhood; no mastoid symptoms until three days ago, when severe shooting pains in the ear and head began. Yesterday had a severe chill, vomited, and was dizzy. Two and a half hours later had another hard chill, and last night had third chill; none to-day. Patient is weak, pale, dizzy, and looks sick. Temperature, sub-normal (97.5°).

*Examination.* Mastoid, no œdema or redness and only moderate tenderness. Meatus, foul discharge. Membrana tympani destroyed; middle ear filled with granulations. No jugular tenderness. Note is made that the external jugular on the affected side does not fill up so well as on the normal side. No optic neuritis. Hearing in the affected ear poor, watch by contact; loud whisper, four inches; speech five inches. Four hours after admission had a slight chill, temperature 102.5°. Operation the following day revealed, on chiselling through the hard cortex, 5 to 10 c.c. of foul pus on the sinus. The sinus wall was thick and of a yellow color, as was also the cerebellar dura. Antrum and middle ear full of pus and granulations. A complete radical was done.

There was some doubt as to whether the sinus was thrombosed, and on account of the fact that the history showed only three days of acute mastoid trouble, it was concluded not to open the sinus until further symptoms appeared. The night following the operation patient had a chill, temperature up to 107°. The sinus was opened, found thrombosed, septic clots removed; free flow of blood from behind the knee, none from the bulb end. The internal jugular vein was therefore ligated and excised. The vein in the neck was not thrombosed, but was ligated and excised in order to prevent the possibility of septic emboli from the clot remaining in the jugular bulb entering the general circulation. Nevertheless, such had already happened, apparently, for septic pneumonia in patches scattered through both lungs followed, from which the patient died ten days later.

The second case was similar, except the history showed chills, fever, and sweats of nine days' duration prior to the curettement of the sinus and ligation of the internal jugular vein. Death resulted.

The third case was that of a baby three months old, admitted with foul otorrhœa, subperiosteal abscess, facial paralysis, and temperature of 104°, and a septic look. Operation revealed mastoid full of pus, cerebellar dura and sinus covered with yellow exudate, so much so that the exact location of the sinus was with difficulty determined. Sinus incised and found thrombosed. The inner wall of the middle ear was necrotic and pus could be seen coming from the region of the oval window. The internal ear was therefore opened, showing pus within cochlea, vestibule, and semicircular canals. Death resulted from meningitis.

Of the remaining 6 cases of sinus thrombosis 4 recovered and 2 died, one of septic pneumonia (case referred to above where the sinus was accidentally opened) and the other of leptomeningitis, following a hernia cerebri that sloughed.

Of the 4 cases that recovered, the internal jugular was ligated and excised in 2 cases because the clot extended down the sinus into the jugular bulb. In both of these cases the neck wound healed quickly, in 1 case by primary union. In the other 2 cases, on cleaning the clots from the sinus, free flow from below as well as above occurred, so the internal jugular was not ligated.

It was worth noting that in all 4 cases that recovered the thrombosis of the sinus had not proceeded to the dangerous stage of septic disintegration of the clot *with the classical symptoms of chills and irregular fever, which show that the danger point has been reached, if not altogether passed.* In each case the thrombus before operation was not diagnosed, although the symptoms pointed, of course, to extensive mastoid destruction. Their histories seemed to show that *in every mastoid of extensive involvement, where necrosis of the sinus groove is found the sinus should be uncovered and carefully examined lest thrombosis may have resulted unheralded by any positive diagnostic symptoms.* Further, that *incision of the sinus wall is in some cases a necessary and conservative procedure in order to determine a diagnosis of thrombosis.* In each of the 4 cases examination of the sinus strongly pointed to thrombosis; and, to determine definitely, the sinus was promptly incised. All 4 cases recovered. It is fair to assume that by delay in opening the sinus in each case until chills, fever, and sweats appeared, a less favorable outcome might have resulted.

Of the 281 cases operated on, perisinuous abscesses were found in 46 cases. Epidural abscesses in 21 cases. It is noteworthy that only 16 of these 67 cases were children (under ten years of age), while of the 72 cases of subperiosteal abscesses 46 were children, indicating the tendency of the suppurative process in children to

extend outward through the thin, soft cortex; while in adults the reverse is the tendency.

Bezold perforation occurred in 7 cases, all but one being adults.

Facial twitching during operation was noticed in one mastoid and twenty-one radical operations. In the mastoid it occurred while removing the tip; whereas in the radical operations it was noticed, as a rule, during the curettement of the necrosed inner wall of the middle ear, in the neighborhood of the oval window.

**RESULTS.** The results of 90 mastoid operations were personally observed as follows: sixty-two made a complete recovery, namely, the mastoid healed with a good scar, the canal discharge ceased, the middle ear inflammation subsided, the membrana tympani regained normal, and the hearing was restored. Nine died. In 7 the mastoid healed with a good scar, but discharge from the ear persisted. In the remaining 14 cases the mastoid did not heal, 9 of which were re-operated.

Of the 62 recoveries the average time required for healing the mastoid was sixty-seven days; 2 healed in less than a month; 15 cases required over three months, and one case required four months, possibly due to lowered vitality from diabetes.

*Hearing.* In 54 of the 62 recoveries the hearing was fully restored. In 5 cases the normal hearing had not been entirely regained when last seen.

Of the 14 cases of failure from the mastoid operation, eleven were babies. No explanation for this large proportion of failures in children is attempted. In fact, this is contrary to the experience of some others who have observed a large number of mastoids and found that in children the results after the mastoid operation were particularly good. As a rule, those mastoids in children healed best in which the mastoid wounds were not sutured but left open. In this series the tendency to excessive and hence unproductive granulation was more marked in children than in adults.

Of the nine deaths after the mastoid operation, five died of meningitis, one from sinus thrombosis, one, a baby, died from the effects of chloroform; and the eighth death was from diabetic coma during the convalescence from the mastoid operation. The ninth death occurred after the patient had left the hospital and was apparently independent of the mastoid, which was doing well. The cause could not be learned.

*Facial paralysis*, occurring as a symptom in 5 of the 164 cases of acute middle ear suppuration, disappeared after operation in all but one case, a five-months-old baby, in which the paralysis persisted when last seen. Facial paralysis brought on by the mastoid operation in 6 cases resulted as follows: in 3 cases (all babies) the paralysis, which was complete, persisted; in the other 3 cases it wholly disappeared in 1 case and was disappearing in the other 2 cases when last seen. It is noteworthy that the 3 cases



where the paralysis persisted were all babies, showing the unusual care necessary in babies to prevent damage to the facial nerve, which in early life emerges from the mastoid relatively high up and superficial.

*The after-treatment* in all mastoids was about as follows: The first dressing was made usually on the third or fourth day. The outer dressing was sometimes removed earlier if it became uncomfortable and a lighter dressing substituted. The frequency of the subsequent dressing depended on the amount of discharge. No irrigation was used, as a rule. Sterile gauze was substituted for the iodoform gauze packing whenever there was a tendency to exuberant granulation, the effort being to fill up the mastoid wound with firm scar tissue. At every dressing the canal was carefully cleaned of any discharge, and the membrana tympani inspected to observe whether the inflammation was properly subsiding. The duration in the hospital after the mastoid operation was as follows: 50 cases were discharged within the first week; 93 cases within two weeks; 10 within three weeks, and only 7 cases were over three weeks in the hospital.

RESULTS AFTER THE RADICAL OPERATION (Schwartz-Stacke or simple Stacke). Of the 117 radical operations the results in 66 are personally known to be as follows: 26 gave apparently perfect results; 20 were progressing well to good results when last seen; 2 were failures, and 8 died.<sup>1</sup>

It should be noted that these include many of the cases where most destructive mastoid involvement was found, following chronic suppurative otitis media; and further, that the radical operation was not considered entirely successful until the mastoid wound healed with a good scar, the middle ear discharge ceased, and the combined mastoid and middle ear cavity became dry, hard and glistening, indicating complete epidermatization.

Of the 26 recoveries, 12 followed radical operations performed solely for the chronic suppurative otitis media, where no mastoid involvement had occurred. Such proved the most favorable cases. Out of 23 such cases where the results were known, in only 3 did failure occur; 8 were progressing well to complete recovery when last seen.

In 4 of the 66 radical operations, a permanent post-auricular opening was purposely maintained in 2 to ensure the permanency of the result, while in the other 2 cases it resulted possibly from too tight packing. Subsequently, in these 2 cases the openings were closed by the plastic operation, leaving a good scar in each case. In all of the 4 cases complete epidermatization resulted.

<sup>1</sup> The remaining 51 cases, including some of the most favorable private cases, were not personally followed up. Therefore, while many undoubtedly made good recoveries, they are not included in the series, the aim being to report only results personally observed. The same is true of the recorded results after the mastoid operation.

*Hearing.* After all the radical operations of this series, the hearing tests, when made, showed as a rule slight if any change in the deafness that had existed before operation. There were a few cases of apparent improvement, but also a few cases of slight decrease in hearing. As a rule, no improvement in hearing was promised.

The length of time after a radical operation before a case was considered cured naturally varied according to whether there was much or any mastoid involvement. The average time from the date of operation, in 22 cases, proved to be three months and seven days. The extremes were 1 case apparently cured in thirty days, while another case took four months. As a rule, skin grafting the middle ear cavity considerably shortened the time.

The cases marked "recovery" after the radical operation were followed up, for periods varying from two and a half to fourteen months, without any return of the aural discharge.

*Facial paralysis* followed the radical operation in 20 of the 117 cases. In 4 the paralysis was complete and persisted, 10 had recovered or were improving when last seen, and 6 cases were lost track of. In 8 cases the paralysis was anticipated by facial twitching during the operation. In 12 cases the paralysis was evident on recovery from the anæsthetic; while in 8 cases the paralysis began to appear later (from the third to eighth day). In such cases the prognosis proved more favorable for a complete disappearance of the paralysis.

Of the 6 cases of facial paralysis occurring before operation, necrosis of the facial canal was found in 3 cases; the other 3 cases were the result of operations performed elsewhere.

*Skin Grafting.* In 37 of the 117 radical operations, skin grafting was done; in 27 cases on completion of the radical, and in 10 cases, at a second operation. The results were as follows: 9 gave almost perfect results, the grafts having taken well; in 14 cases the grafts took partially; in 6 cases the grafts failed to take, and in 8 cases results were not observed. The results in the cases observed in this series indicated the value of skin grafting on completion of the radical operation by hastening epidermatization of the middle ear cavity.

In the other radical operations in this series it must be noted that as perfect results were obtained without skin grafting, but only in those cases that were patiently dressed for a long time, and where tight packing of the middle ear cavity with little pledgets of gauze was persistently adhered to.

Death followed the radical operation in 8 of the 117 cases. One died suddenly on the table, apparently from ether poisoning; 1 from leptomeningitis, cause unknown, unless through suppuration of the internal ear. Autopsy was not permitted. The other 6 fatal cases were those of chronic suppurative otitis media, in

which extensive mastoiditis had rather suddenly developed; 3 from thrombosis of the lateral sinus, and the other 3 from meningitis. Their histories were given above.

These 6 fatal cases indicate the ever-present danger from a chronic suppurative otitis media. This is also emphasized, by a glance at the histories of the cases of sinus thrombosis, 7 of the 9 resulting from chronic ears.

The total number of deaths was 17 in 281 operations, a mortality of 6.5 per cent.

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## THE EFFECT OF SUPRARENAL PREPARATIONS ON LIVING PROTOPLASM.

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As a clinician working constantly with various extracts and derivatives of the suprarenal gland in nose and throat work, I have noticed repeatedly that besides the physiological action which we find regularly demonstrated as the result of the use of this class of remedies there are also certain detrimental effects which are coming more and more conspicuously to the front the more we work with these preparations, and the more we are able to contrast our former experience before supranenal derivatives were used with our present experience where we use them almost invariably.

There are certain unfavorable clinical effects which I have noticed coincident with the use of suprarenal solutions which seemed to me to be present because they were used. One reason for this view is that we never saw such conditions before these medicaments were brought into use; and another is that these unfavorable conditions are on the increase rather than on the decrease despite our attempts to control the results without eliminating the effects of the suprarenal preparations.

These doubtful results are:

Hemorrhage.

Reactionary symptoms.

Swelling and localized areas of œdema.

Retarded healing.

Sloughing.

Unhealthy condition of wounds.

It is with the object of throwing some light upon the possible causative relations of suprarenal preparations to these conditions that this research has been undertaken. The experiments enumerated in this paper may be divided under five classes:

1. Experiments to establish the effect on the clotting of blood, with the hope of explaining some causes of secondary hemorrhage.

2. Experiments to establish the effect on living protoplasm, to explain, if possible, delay of healing.

3. Experiments to ascertain the effect on muscle tissue so that we may understand the contractile effects of this remedy on circulation and if possible to classify this effect, either the result of a nervous or muscular stimulus or an admixture of both.

4. Experiments to ascertain the limit of dosage to produce—

(a) No effect on life processes.

(b) A decided effect on life processes, but one from which recovery may ensue—*e. g.*, poisoning.

(c) A decided effect on life processes, but one from which there is no recovery—death.

5. A set of experiments to ascertain if immunity is an inherent property of protoplasm, or if immunity to it can be developed.

**EFFECT ON CLOTTING.** The blood of the starfish was first used for this experiment. It will be remembered that the clotting of the circulating fluid in this cold-blooded animal occurs slowly, after the lapse of an appreciable period of time, by means of fibrin fibrillæ, or protoplasmic projections, which form around the bodies of the white blood corpuscles. By some investigators this phenomenon is considered to be a protoplasmic derivative from the corpuscle itself. The corpuscle is supposed to send out protoplasmic projections; but there seems to be no evidence to support this fact.

For the purpose of our discussion it is easier to assume that fibrin is deposited from the serum by the action of some enzyme produced by the action of the white blood corpuscle. This phenomenon correlates better with what we know of the coagulation process as it occurs in the higher forms of life.

If a specimen of starfish blood be dropped from the animal upon a microscopic slide at the ordinary temperature of the room, it will require about forty minutes for complete coagulation to occur. If now the blood be dropped from a starfish (*asteria*) immediately into a solution of 0.0001 adrenalin in sea-water and examined immediately, the fibrillæ of the fibrin around the white blood corpuscles will be seen to have formed completely and immediately. In other words, the coagulation process in the starfish is accelerated. The clotting seems to be normal. The clot is well formed, and the time required is decidedly shortened.

Another effect is produced by increasing the strength of the solution to 0.001. If into such a solution some of the blood of the starfish be dropped and immediately examined, nowhere can fibrin be seen attached to the white blood corpuscle nor extending throughout the serum, but on the other hand there seem to be changes established within the white blood cell itself. The cell is swollen and appears to be partitioned off by fibres which have developed within its body—for these can be seen highly refractive and extending throughout the body of the corpuscle. The spaces between

these fibres have a microscopic appearance of vacuolization. They appear less refractive and shaded, and seem to have absorbed water into the vacuoles which have formed as the result of the exposure to the suprarenal preparation. These experiments were repeated many times with invariable results; and it may be stated as the result of the observation of the clotting of blood in a starfish that in solutions of 0.0001 the phenomenon of clotting is accelerated, but otherwise is normal; while blood placed in a solution of a strength of 0.001 shows three very decided changes:

1. The process of fibrin formation is interfered with.
2. The white blood cells become changed in character and vacuolization occurs.
3. The phenomenon of clotting does not occur.

When another animal is chosen for the same experiment and the blood of a horseshoe crab (*limulus*) is used, the same phenomenon is observed. If the blood of the *limulus* is received in a 0.001 solution no clot will form and no fibrilization of the white blood corpuscles can be demonstrated. The blood of another cold-blooded animal, the sea-urchin (*arabacia*), was also used, as well as the blood of fundulus or sea minnow, and turtle and frog blood. These different bloods were separately subjected to the activity of a 0.001 solution, but the clot in each instance was found to be normal. The phenomena of clotting was not changed as in the other experiments, nor did the clot soften and dissolve if the immersion in the suprarenal solution was continued.

It seems fair to conclude as the result of these experiments that solutions in the strength of 0.001 interfere with the phenomenon of clotting of blood in some of the cold-blooded animals (*asteria* and *limulus*), but that in other animals there is no change.

If these results can be applied to warm-blooded animals we may assume that the active principle of suprarenal gland has no effect upon the coagulation phenomenon, and that the danger of secondary hemorrhage from softening of the clot is not increased by its use. The fibrillation within the body of the white blood corpuscle noticed in the *asteria*, where the corpuscles seemed to be disorganized, was not confirmed in the experiments on other forms.

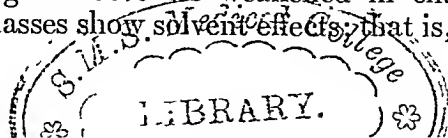
**EFFECT ON SPERMATOOZOA.** The living spermatozoa form a convenient object for experiment with which to ascertain the effect upon the motion of rapidly moving cells. Under normal conditions the spermatozoa of starfish or sea urchins will remain alive in sea-water at the ordinary temperature of the room for hours, slowly deteriorating, but for a long time retaining their activity and their power of motion and of penetrating the ovum. The vitality of the spermatozoon is directly proportional to its ripeness. It is most active and resistant to death processes when it is ripe or ready to be discharged by the animal into the sea-water. A marked difference in the activity of the spermatozoa can be seen the moment

these bodies are brought within solutions of sea-water containing a solution of the suprarenal gland. A full description of these experiments is not necessary, but briefly, if the ripe spermatozoa of the asteria (starfish) are discharged into solutions of sea-water and adrenalin 0.0001 the motion of these bodies is immediately lessened, their activity retarded, and in two hours they lose all their power of motion and penetration; that is, the organism dies. If the active spermatozoa are brought into solutions of sea-water of a much weaker strength, 0.00013, the motion of the spermatozoa is immediately checked, but recovery of motion occurs in the course of fifteen minutes, when their normal activity seems to be resumed as well as their power of penetrating the ovum.

In these two experiments it will be seen that solutions of the strength of 0.00013 influence the activity of these bodies immediately, but the dose is only temporarily effective, recovery from the exposure taking place in a short time. On the other hand, these spermatozoa if exposed to a solution of 0.0001 are poisoned so that they never recover. If these bodies are placed in a 0.001 solution their motion is immediately lost, and in the short space of six minutes their activity is permanently impaired and they die.

Another set of experiments was made with spermatozoa of *arbacia* (sea-urchin). If the ripe spermatozoa from these animals is brought into a solution of sea-water and the active principle of suprarenal gland of the strength of 0.0001 the same phenomenon is observed and they die within two hours. Brought within a solution of the strength of 0.001 they die immediately. Further experiments, the details of which need not be narrated here, indicate that a solution of 0.0005 is a fatal dose for the spermatozoa, immediately causing cessation of motion and death within a short period. It is interesting to see the manner in which these rapidly moving protoplasmic cell derivatives are affected physically by it. The phenomenon is analogous to the coagulation and clumping phenomenon with which we are familiar in the reaction of the typhoid bacillus. The first effects of these solutions appear to be a cessation of the motion of the body of the spermatozoa while the flagellæ continue to move. The first change of motion of the flagellæ brings the heads of the spermatozoa into contact, and after this is effected the bodies do not separate. The grouping produces the clumping, and the size of the clump particles is increased by the continuous bombardment of other spermatozoa, which as soon as they touch the clumps seem to adhere to the main mass and to be unable to separate themselves from it.

The next change is an agglutination phenomenon. The bodies seem to lose their distinctively individual character and to fuse together. During this time the motion of the tail of the spermatozoon continues, although it becomes weakened in character. After a while the fused masses show solvent effects; that is, the spermatozoa



disappear as individuals and the bodies fuse together, forming a clump of protoplasm in which the histological features of the individual bodies are lost.

Dr. Albert Matthews, who observed this phenomenon with me, expressed the opinion that this effect seemed to be produced by an action of the drug on the nuclear body within the spermatozoon. The interpretation of the effect in weak solutions upon the spermatozoa of the starfish and sea-urchin is that this alkaloid has direct detrimental action on the protoplasmic activity of these bodies.

**EFFECT ON EGGS.** For these experiments the eggs of the *arbacia* (sea-urchin) were used. These were selected for their convenient size, the fact that at the time of the year when these experiments were undertaken the eggs were ready to be fertilized, and because changes in their microscopic character are easily discernible with a low power lens. Under normal conditions, when the eggs of the sea-urchin are brought into contact with the spermatozoa and the material kept in fresh sea-water at the ordinary summer temperature of a room, fertilization immediately takes place and the impregnated ovum in the course of time regularly undergoes its characteristic segmentation and development. This, as we all know, consists in the regular segmentation of the ovum into two, four, eight, sixteen cell stages, and then to the morula and gastrula type of ovum, in which the embryo takes a swimming form, becomes an individual being, and soon afterward leaves the embryonic stage and develops the adult type. The time which this requires depends much upon the temperature of the water.

A number of eggs were fertilized and used as control in order to check the results in the eggs which were put under abnormal conditions. Under fairly normal conditions in the control experiments, the segmentation of the egg required fifty minutes for the two-cell stage; seventy to one hundred minutes for the four-cell stage; one hundred and twenty-five minutes for the eight-cell stage; one hundred and sixty minutes for the sixteen-cell stage. The morula stage was reached in four hundred and fifty minutes, while an average gastrula was developed in one thousand four hundred and forty minutes. In all of these types the swimming form was apparently normal. The animals were not developed to adult forms.

The multitude of experiments which have been made by Jacques Loeb and Albert Matthews regarding the effect of certain solutions of different osmotic pressure upon the eggs of low forms of life, show that these cells are exceedingly sensitive and react to slight differences in osmotic pressure. It is not necessary in this article to narrate any of their experiments, but the reading is so fascinating and the results so remarkable—while the teaching from these results may be applied to the action of different strength solutions upon the cell existing within the human body—that I earnestly

recommend all my hearers to go over the literature of these experiments. Besides, it is interesting reading and serves to introduce some new ideas as to the effects of therapeutic remedies upon cell activity.

In my experiments with these eggs I subjected them to solutions of the active principle of suprarenal glands in a normal saline solution, so as to reproduce the conditions under which we use the drug within the body, but the differences of osmotic pressure between the normal saline solution and the sea-water were so great as to disintegrate the eggs, produce twin or extra-ovate forms of fertilized eggs, stimulate ciliary movement, and hasten cleavage at all stages of their exposure within these saline solutions, so that it was necessary to develop them in sea-water. Even the small quantity of chlorine which is present in the muriate of adrenalin so disturbed the osmotic pressure of the solution that the results of the experiments were not trustworthy, nor could they be said to be under normal conditions. It was therefore necessary in these solutions to dissolve the alkaloid in sea-water and to use various strengths of this solution for experimental purposes. When this was done, the differences of osmotic pressure vanished and the eggs behaved as if they were under fairly normal conditions. Hundreds of these experiments were carried out, and the results which are here given in a tabulated form are average results for a set of experiments; and the conclusions which are deduced are from the total number of experiments and not from any single set.

It will be necessary now to digress somewhat and spend a few moments in considering the normal development of sea-urchin eggs, in order that we may better understand the effect of the suprarenal gland extracts upon them. Under normal laboratory conditions, if the ripe eggs of the sea-urchin be mixed with the spermatozoa from the male no changes will be apparent for some time except the polarization of the egg. The first microscopic evidences are exhibited in about forty minutes after fertilization when clefts are seen to form on opposite sides of the egg, which gradually merging segment the egg. This process is completed in about fifty minutes. After a period of apparent rest, each of these segments divides, producing an egg with four segmentations instead of two. This is called the four-cell stage, and is completed from in seventy to one hundred minutes after impregnation. This process of division of each of the cells within the egg continues to the eight-cell stage, which is completed in about one hundred and twenty-five minutes; then to the sixteen-cell stage, which is completed in about one hundred and sixty minutes. The subsequent division of the cells is not easy to observe. The next convenient stage for observation is the morula stage, which is ordinarily completed in four hundred and fifty minutes after impregnation; and the gastrula stage which succeeds the former is ordinarily completed in one thousand four hundred and forty minutes.



When the eggs of the sea-urchin are fertilized and then developed in solutions of the active principle of suprarenal gland, marked differences in the time of the development of the eggs are seen, according to the strength of the solution, and a rather definite line can be drawn where eggs thus exposed go on to fairly normal development although markedly retarded, and where eggs are killed by the solution. A glance at the following table will show the effect of solutions of adrenalin of different strength in retarding or killing the eggs of the sea urchin.

ARBACIA EGGS FERTILIZED IN SOLUTIONS OF ADRENALIN AND  
SEA-WATER.

Division of egg represented in minutes.

	Strength of solution.	2-cell stage.	4-cell stage.	8-cell stage.	16-cell stage.	Morula stage.	Gastrula stage.	Swimming stage.
Poison zone	0.001	140	190	230	dead	dead	dead	dead
	0.0002	125	140	245	330	dead	dead	dead
	0.0001	100	147	245	300	dead	dead	dead
Zone of marked retardation	0.00005	50	95	165	207	555	1440	normal
	0.00008	50	75	127	170	555	1440	normal
	0.000001	60	75	125	165	555	1440	normal
Zone of slight retardation	0.000002	60	75	125	160	520	1440	normal
	0.000003	50	75	125	160	500	1440	normal
Control	.....	50	70-100	125	160	450	1440	normal

A glance at this table shows that if eggs of arbacia are fertilized and developed in solutions of the active principle of suprarenal gland and sea-water they behave:

1. As does the control in solution of less than 0.000001.
2. That the development of fertilized eggs is retarded but slightly when the strength of the solution is less than 0.0001 and more than 0.000001, and that the eggs recover from the retarding effect and develop normally.
3. That these fertilized eggs are killed in the sixteen-cell stage, and are retarded in their development in all stages when the solutions are less than 0.001 and more than 0.0001. This observation is important because they are the solutions which we use in medicine.
4. That these eggs are killed in the eight-cell stage and retarded in their development in solutions of 0.001 or stronger.

A study of the results of these experiments shows that such solutions in sea-water are very active upon the sea-urchin egg; may kill the protoplasm if the solution is strong enough; or if the solution is somewhat weaker it has a marked and regular effect in preventing the cell division and development of the egg. It also shows that at a certain stage in the cell division of the egg, the protoplasm is changed so that it never develops further. In weaker solutions the

cell division of the egg is interfered with, and while the development of the egg is not stopped it is markedly and very regularly retarded.

From these effects upon the sea-urchin's egg, it seems fair to assume that the same effects may be active in the human individual, since the properties of protoplasm are much the same wherever it is found. If this be true, then we may assert that suprarenal preparations have a marked effect on cell division of healing tissue and upon the proliferation of cells constituting granulation tissue. It may also be assumed that these solutions will have an effect depending on the strength of the solution as well as the duration of the exposure, and that it is possible to kill cells or to prevent their activity, or retard cell division. In this connection it should be remarked that other substances, especially alkaloids (atropin and aconite), seem to act similarly.

**IMMUNITY.** A number of experiments were performed to determine whether an immunity to the poisonous effects of adrenalin could be developed in the fertilized egg. These experiments failed to establish the fact of the development of immunity, but on the other hand they showed that the protoplasm was decidedly weakened by development in weak solutions. It is not necessary to narrate the details of these experiments, but it was shown that if the eggs of the sea-urchin were fertilized and developed in weak solutions (even such a weak solution that it would not markedly retard the time of development of the egg), they did not develop any immunity to the poisonous effects of stronger solutions. The eggs of those developed in sea-water when put in a poisonous solution would live longer than those that were developed in the weak solutions.

Furthermore, it was shown that the rate of progression of the moving ciliated ovum was much slower in cases that were developed in weak solutions. To my mind these two facts prove that the vitality of the protoplasm is weakened by suprarenal solutions. The application of this fact to the human organism is apparent and does not require elaboration at my hands.

**EFFECTS ON CILIA.** The effects upon cilia are among the most interesting results of these experiments, and apparently have a direct application to the effect of this drug on man, since the mucous membrane of the respiratory tract where this drug is so constantly used is lined with epithelium of the ciliated variety.

It will be remembered that in early forms of embryonic life the various sea animals develop cilia upon their external surface as soon as they reach the gastrula stage; by means of these cilia, long or short, they propel themselves through the water. The cilia in the sea-urchin and in the starfish embryos are not so numerous but that they can easily be observed with a medium power microscope, and the long cilia of the aroncula (sand-worm) larva can be very easily and satisfactorily studied. It is also to be remembered that the ciliated processes on epithelium are not supposed to be

separate structures from the protoplasm of the cell, but are considered to be protoplasmic prolongations covered with ectoderm, so that the effect of adrenalin upon the cilia is really an effect upon the activity of the protoplasmic contents of the cell.

A great number of experiments were carried out upon the larva of the sea-urchin, starfish, and aroncula, and these experiments were repeated many times, with constant results. Other experiments were made with the cilia found on the gill of the clam and on the trachea of the frog.

When the eggs of the sea-urchins were studied it was found that when they were in the blastula stage under fairly normal conditions they moved so rapidly over the microscopic field that they required only about five seconds to cross it. As soon as they were brought into solutions of the active principle of suprarenal gland and sea-water a marked effect on their rate of progress was observed, and this effect was directly proportional to the strength of the dose. If the strength of the solutions in which these animals are placed is 0.001 there is an immediate slowing and almost a cessation of the ciliated movement by means of which the blastula progresses, and the same animal requires three hundred seconds to cross the microscopic field, where under ordinary conditions the same distance would be traversed in five or ten seconds. If the strength of the solution is 0.0002 it requires one hundred and twenty seconds to cross the field. If the strength of the solution is 0.0003 it requires twenty seconds to cross the field, showing that the animal is not affected markedly by this strength of solution, while with a solution of 0.0002 there is a distinct retardation. In other solutions weaker than 0.0005, the effect upon the motion of the animal is almost imperceptible. Some few batches of developing embryo were slightly affected by solutions as weak as 0.00002. It must be remembered that these effects are immediate and that they show distinct and specific result upon ciliated movement. When the same embryos are exposed for longer intervals, they are either killed or in very weak solutions their movements are markedly interfered with; while in the control the embryos appear to be normal. For example, the *arabacia* blastula were exposed to solutions in sea-water for ten hours and were then examined. In varying solutions of the strength of 0.001 to 0.00005 all movement in the blastula had ceased and the animals did not recover when returned to sea-water. In solutions weaker than this—for instance, 0.000001, after an exposure of ten hours—there were a few slow-moving forms, but most of the embryos were killed. When the embryos which were moving were put again into sea-water they continued to live, although they never recovered the power of rapid motion. In solutions of 0.000002, after an exposure of ten hours, the ciliated movement was rather active and remained so. These animals recovered and developed normally when returned to sea-water. In

solutions of 0.000003 a very different reaction was found—indeed, the animals seemed to be stimulated by the solution and moved more rapidly in it after ten hours than they did in the control with sea-water. It is interesting to note this fact, that in solutions of 0.000003 there was an increase in the activity of the ciliate movement over the normal, while in other strength solutions there was a decrease.

**EFFECT ON ARONICULA LARVÆ.** The embryonic form of this animal is convenient for examining the effect of adrenalin on ciliated and muscular movements, and the results can easily be investigated.

It will be remembered that this embryo of the sand-worm consists of a body of protoplasm about three times as long as it is wide, and that its movement is a combination of ciliated and vermicular progression. The cilia are distributed throughout the whole body of the animal in the form of short, hair-like processes, but near the head and tail they are collected in a fringe-like collar, where they are much longer than those over the other parts of the animal. A very rapid rate of progression is produced by the waving of the cilia, and particularly by means of the elongated cilia, the movements of which can easily be studied.

Another movement is produced by muscular contraction. Bands of longitudinal muscular fibres run from the head to the tail of this animal and produce quite a different form of movement from the ciliated variety. When the muscles are active, the body of the animal is contracted or elongated, and a slow vermicular progression results. When the cilia are active, the movement is very rapid and without vermicular contraction.

These two methods of movement give us a good opportunity to study the effects of suprarenal preparations upon both the cilia and the muscular fibre. Besides this, the animal is very strongly attracted to the light—that is, it is heliotropic. These animals exhibit the most beautiful light reactions, for when they once attain a sufficient amount of light to satisfy their reaction they will remain indefinitely in the light; while if they are placed in the dark and the light is concentrated at a certain point in the vessel in which they lie, they will swarm rapidly toward the point of light. Now if the ciliate movement is interfered with, the heliotropic reaction remains as active as before, but the animal moves less rapidly toward the light by means of muscular effort alone. The rate of progression may be studied with the naked eye and with a low power lens.

In this connection it is interesting to note the effect of suprarenal preparations upon both the muscles and the cilia of this embryo, and it is, of course, to be remembered that the results were always compared with control animals kept in normal condition.

If the aronacula larvæ were transferred to solutions of the alkaloid of suprarenal gland and sea-water of the strength of 0.001, and examined under a low power microscope, in five minutes the ciliated

movement was markedly retarded; and if again examined after five hours all ciliated movement was checked and the animal did not respond to the heliotropic reaction. The animal was at once strongly contracted, assumed a ball-like shape, and remained in this condition. All muscular movement was not abolished at once. There was a sluggish vermicular movement by means of which the animal made some progression toward the light, but in five hours even this slight movement was lost.

In solutions of 0.0002 the same effect was observed; in solutions of 0.0003 and 0.0005 the cilia slowed immediately, and in six hours there was a slight heliotropic reaction. The effect on the muscle tissue was as immediate as in the strong solutions. The animal contracted into a ball at once, and by very slow vermicular movements, especially by twisting at its posterior end, progressed very slowly toward the light. All muscular movement in the animal ceased after six hours.

In solutions of 0.00001 the effect was quite different. At the end of five minutes the movements of the cilia were normal and the animal progressed toward the light at its usual rate of speed. After one hour the ciliated movement seemed to be stimulated, and the rate of progression increased, but in five hours the cilia had stopped all movement. The muscular effect in this strength of solution (0.00001) was also normal for five minutes and afterward became gradually slowed. It remained slowed for three hours and finally stopped. It will be noticed that in this solution the muscular movement ceased before the ciliated, the muscle acting for three hours, the cilia for five hours.

In solutions of 0.00005 the ciliated progression remained normal at the end of five minutes, and at the end of five hours was slowed but not stopped; the muscular movements five minutes after submersion were normal, but ceased after five hours.

In solutions of 0.00003 the cilia were normal until three and a half hours had elapsed, when they ceased their activity; in solutions of 0.00008 the heliotropic reaction was apparent for the same length of time. In both these solutions the heliotropism seemed to be increased and the muscular movement seemed to be stimulated, and this continued for about three and a half hours, when their reaction to light became diminished and the vermicular movement was partly checked.

In solutions of 0.000001 the ciliated progression remained normal for two and three-quarter hours; then the cilia became slower but not checked. The muscular movement remained normal for two and three-quarter hours, when it became slower but was not stopped.

INTERPRETATION OF RESULTS. The result of these experiments expressed briefly is that the cilia of the aroncula larvæ are affected only by stronger solutions than are necessary to paralyze muscle

movement. In interpreting these results we again see a clear line of demarcation drawn between the strength of solutions. These slight differences show a potentiality which we would not suspect. For instance, the ciliated movement was slowed in all exposures of 0.00001 to 0.00003, while in all solutions weaker than 0.00008 the ciliated movement remained normal. This is something like the line which we were able to draw in interpreting the effects of suprarenal preparations upon the development of the *arbacia* egg.

These experiments also show that the cilia are more easily affected than cell division.

Experiments were also carried out with the cilia on the gill of the salt-water clam. These are very active cilia, working on the surface of the respiratory filter and throwing sea-water containing protozoa and other nutritive material into the interior of the clam.

When these cilia were brought into suprarenal solutions of sea-water of the strength of 0.0001, the motion was slowed in ten minutes, distinctly weaker in twenty-five minutes, and very feeble in fifty minutes; but solutions of this strength did not produce a cessation of the movement of these cilia; even after twelve hours the cilia were moving, and had partially recovered from the enfeebling effects which were shown earlier. The movements generally were slower at the end of twelve hours than in the normal specimens, but they still fulfilled their physiological purpose.

It would seem as if these cilia were more resistant to the effect than those of *arbacia* or *aronicula*, and this we might expect in an adult animal.

The next experiments were carried out on the cilia of the *œsophagus* of a frog. The *œsophageal* membranes were placed in a solution of 0.0001, and the immediate effect was to produce a slowing in the ciliated movement. These cilia were also more resistant to the effect of this solution than *arbacia* or *aronicula*, and it was not possible to entirely check the action of the cilia with solutions of 0.001.

**EFFECT ON CONTRACTILE TISSUE.** The turtle heart was chosen to study the effect upon the contractility of muscle tissue. If the entire heart of the animal, which was removed from the body, was placed in a normal saline solution and allowed time to rest and recover its natural beat, it was found after an interval of two minutes in which the beats were not counted, to beat in successive minutes thirty-two, thirty-two, thirty-six, thirty-seven, and thirty-seven times. The same heart was then transferred to a suprarenal preparation of the strength of 0.001 in salt solution, and after a proper interval, in which no observations were made, the same heart beat in successive minutes thirty-six, thirty-six, thirty-six, thirty-six, forty, forty, thirty-two, thirty-two, thirty-two, thirty, and thirty times, and from then on gradually ceased its beating. The contraction became less frequent and weaker. This shows a slight

increase of beat after the muscle was brought into adrenalin solution.

Another heart, which was placed in distilled water, beat in successive minutes nine, nine, ten, and thirteen. The same heart when placed in suprarenal alkaloidal solution and distilled water of the strength of 0.001, beat in successive minutes thirteen, twelve, thirteen, thirteen, fourteen, and thirteen times per minute.

A very interesting experiment was made with another turtle heart. This heart was removed from the body and allowed to remain exposed to the air until it had ceased to beat. It was then placed in distilled water, where in four minutes it had not beat at all and remained relaxed. It was then carefully transferred to a solution of distilled water and an alkaloid suprarenal preparation of the strength of 0.001, when it immediately began to beat, in successive minutes beating four, twelve, fifteen, fifteen, and seven times. The systole was long and strong. The relaxation of the heart in diastole was extremely short.

Does not this show a decided muscle stimulation from suprarenal solutions?

Another heart which was kept moist and exposed to the air, beat in successive minutes forty, forty, and thirty-eight. It was then transferred to distilled water when it beat forty, forty, and forty. It will be noticed there is no increase of the beat. The same heart was then transferred to a 0.001 solution of an alkaloid suprarenal preparation, and the beat increased to forty-seven, fifty-one, forty-seven, and forty-two. Again we see the same strong stimulating effect on the muscle.

The ventricles of the turtle heart were separated from the auricles. It is supposed that the ventricle of the turtle heart is without nerve elements and that it could be used to demonstrate the effect of direct stimulation on the muscle itself without the intervention of any form of nervous structure. At any rate, as soon as the turtle's ventricles were separated from the auricles where the heart ganglia are distributed, it lay in the dish exposed to the air entirely at rest and made no attempt at contraction. When such a nerveless heart muscle was immersed in an alkaloidal suprarenal solution of the strength of 0.001 it begins to beat at once, and in successive minutes beat fourteen, six, and three. Another heart prepared in the same way, which also remained when exposed to the air entirely at rest, beat after being placed in the same solution in successive minutes seventeen, nine, eleven, six, six, ten, and nine times. This appears to show the power of suprarenal gland preparations to cause muscular activity without the intervention of any nerve tissue. The auricles of the same animal, which contain nerve ganglia, when brought under similar conditions beat regularly when exposed to the air thirty-one, thirty-one, and thirty-one times in successive minutes. When placed in suprarenal solution they

immediately increased their beat to thirty-nine, fifty, and forty-eight, after which there was a gradual cessation in rapidity. Again we see the effect of a powerful muscle stimulant.

The thoracic shell of the turtle was removed in such a way as not to open the pericardium or the peritoneum. The whole membranous wall of the exposed surface was bathed in a normal salt solution to restore the blood pressure which had been reduced by hemorrhage, and after twenty minutes the heart in five successive minutes beat sixty-one times. At this time 2 c.c. of a 0.001 solution of alkaloid preparation of suprarenal gland in a normal salt was injected into the peritoneal cavity. After five minutes the beats were again counted. They were more regular than before, and five minutes after the injection into the peritoneal cavity the heart beat one hundred and forty-four times in five minutes. After half an hour in which the animal was completely at rest, the heart beat one hundred and forty-five times in five successive minutes. This shows an increase due to adrenalin of from sixty-one beats under fairly normal conditions to one hundred and forty-five beats in five minutes—another evidence of its powerful stimulating effect. After three hours the effect seemed to be lost and the heart had resumed its normal number of beats—that is, sixty-one beats in five successive minutes.

The thorax and abdomen of a frog were opened and were pinned in such a way as to make a cavity at the bottom of which the heart was beating. Under the condition of exposure to the air the heart beat fifty times per minute. Into this tissue tube, at the bottom of which the heart lay exposed, a solution of suprarenal alkaloid of the strength of 0.001 was poured, and the heart-beat immediately increased to fifty-eight beats per minute. The diastole was considerably shortened, the systole was markedly lengthened, and the entire muscular activity of the heart was immediately increased. It appeared to be beating four or five times its former strength. After two hours it was beating very forcibly and tumultuously, with unusually strong contractions and about forty-eight beats per minute. After four hours it was still beating quite forcibly.

All of these experiments show that suprarenal solutions are powerful muscle stimulants.

**EFFECT ON MEDUSA.** The medusægonionemiæ is well organized for experiments relative to contractility. It is like a jelly fish, but is much smaller. It is bell-shaped and transparent. The rim of the bell contains all the nerve elements, and from this part tentacles depend in which sense organs are developed. The body of the animal is contractile, but does not contain any muscle tissue which can be demonstrated as such. It swims through the water by repeated contractions of the bell. It is claimed that the body of the animal contains no nerve tissue; all the nerve structure is contained in a nerve ring on the margin of the bell-shaped body, so that



the contractile body may be readily separated from the nerve ring with a fine pair of scissors. Ordinarily the movements of this animal are rather slow, the contractions succeeding one another after a slight period of rest.

When these animals are retained in sea-water under as normal conditions as the laboratory will permit, they exhibit periods of activity and of rest. The number of contractions which they make per minute is exceedingly variable, but it may be said that under fairly normal conditions they vary from one to ten per minute.

When these animals are brought into solutions of the active principle of suprarenal glands dissolved in sea-water their conduct is immediately changed. If the dose is strong the body immediately becomes hazy, the bell contracts only once and remains contracted. It shrinks decidedly in size and becomes furrowed and wrinkled, and the tentacles undergo immediate contraction, so that they are curled tight against the body like a ball and the animal dies in this condition. If a weaker solution is used, the animal is immediately stimulated to powerful contractions and enters a state of convulsions from which it may recover if the dose of adrenalin is not too powerful. In this case the body of the animal gradually becomes hazy, the tentacles contract tightly, and finally the animal dies.

If the animal is placed in a still weaker solution, it is immediately stimulated to contraction, but will remain alive and will recover from the effects of the solution if taken from it and replaced in plain sea-water. While it is in this weaker solution it undergoes periods of activity and of rest. It is powerfully stimulated to contract, the number of contractions per minute varying. Sometimes the animal projects itself rapidly through the solution by repeated contractions; at other times its movements become convulsive, in which there may be a tonic contraction lasting for twenty or thirty seconds, or the convulsion may be clonic—the entire body of the animal vibrating incessantly while in contraction. This convulsive state lasts sometimes for a few seconds, sometimes for two hundred seconds. After this exhibition the body of the animal relaxes and it undergoes a rest period of from ten to sixty seconds, after which the increased contractions begin again and continue as before.

It will be seen that the suprarenal alkaloid is a powerful stimulant to contraction in this animal and affects the contractile tissue in a most characteristic and marked way. It was found that the animal reacted best in a solution of the strength of 0.0005. A number of average-sized animals were placed in as normal a condition as possible in quiet jars of sea-water. Their contractions under these conditions were counted for periods of five minutes. Some animals made no contraction during this period and others made as many as one hundred and twenty. The average of these contractions for ten animals was forty-two in five minutes. The

animals were then placed separately in solutions of 0.0005 and the contractions were counted. These varied from ninety-seven to more than nine hundred. Expressed in an average we may say that in five minutes under the influence of suprarenal solutions these animals made four hundred and five contractions in contrast with forty-two in a normal condition.

The animals were then taken from the solutions and were placed in fresh water, and their contractions were again counted over a period of five minutes. These varied from no contractions to thirty-six. All the animals recovered.

The effect of these solutions is well seen in the following table:

#### MEDUSÆ IN ALKALOID SUPRARENAL PREPARATION AND SEA-WATER.

Strength of solution 0 0005. Period of observation five minutes.

	In sea-water.	In alkaloid and sea-water.	In sea-water after contraction.	Recovery.
1 . . . . .	108	356	9	Yes
2 . . . . .	22	413	2	"
3 . . . . .	0	909	1	"
4 . . . . .	95	500	0	"
5 . . . . .	5	600	36	"
6 . . . . .	10	97	30	"
7 . . . . .	10	550	0	"
8 . . . . .	68	294	55	"
9 . . . . .	0	132	0	"
10 . . . . .	120	200	0	"
Average . . . . .	42	405	13	

Are we not warranted in asserting that suprarenal preparations, at least in these lower animals which we have studied, has a tremendous influence on the power of cell division, on the development of protoplasm, on the movement of cilia, and on contractile tissue?

# THE INFLUENCE OF SUPRARENAL EXTRACT UPON ABSORPTION AND TRANSUDATION.

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IN experiments on frogs suprarenal extract seemed to have a distinctly delaying influence upon the toxic effect of strychnine. The following abbreviated protocol of one experiment will illustrate it.<sup>1</sup>

*Experiment 1.* Frog 1 received an injection into the dorsal lymph sac of 0.03 mgm. of strychnine nitrate + 0.7 c.c. pure adrenalin (mixed in the syringe). Frog 2 received 0.03 mgm. strychnine nitrate + 0.7 c.c. normal salt solution (also mixed in the syringe). Frog 2 had the first tetanus twenty minutes after the injection, while in frog 1 the first tetanus appeared seventy minutes after the injection.

In this experiment the tetanus in the animal which received suprarenal extract with the strychnine was delayed fifty minutes.

An extensive variation in the mode of administration of suprarenal extract showed that a delay of the effects in frogs was produced only when the extract and strychnine were brought into close contact: either mixed together in the syringe before injection, or both injections made into the same place. No perceptible delay in the toxic effect of strychnine was noted when the two substances were injected into different localities of the animal.

The delaying effect of suprarenal extract could be explained by a biochemical interaction between it and the strychnine; it could be explained by the impaired absorbing capacity of the tissue, blanched by the extract. To solve these problems we made several series of experiments on rabbits. However, while our investigation was already quite far advanced we discovered that the same subject was treated in two very recent publications by Alfred Exner. We shall, therefore, before continuing the report upon our own experiments, discuss the findings of this author and the interpretations he gives to them.

In the first series of experiments Exner<sup>2</sup> injected adrenalin into the peritoneal cavity of rabbits and guinea-pigs and subsequently injected strychnine nitrate into the same place. In nearly all the

<sup>1</sup> For the lack of space very few protocols will be quoted in this paper.

<sup>2</sup> Zeitschrift f. Heilkunde, 1903, Abteilung Chirurgie, p. 302.

cases there was more or less retardation of the toxic effects of strychnine. Similar results were obtained in experiments with potassium cyanide and physostigmine. In other series of experiments substances were introduced into the peritoneal cavity which appear in the urine, where they are easily recognizable. Urine was obtained by expression of the bladder. It was found that the previous intraperitoneal injection of adrenalin retarded somewhat the appearance of sodium indigo-sulphate and sodium salicylate in the urine, but had no perceptible effect upon the appearance of potassium iodide. Furthermore, after an intraperitoneal injection of an emulsion of paraffin and mucilage the presence of a small quantity of paraffin in the blood could be demonstrated, and Exner states that after a preceding intraperitoneal injection of adrenalin the quantity of paraffin present in the blood was much less. Since the emulsion of paraffin could be absorbed only through the lymphatics, Exner comes to the conclusion that adrenalin impairs the absorption by the lymphatics, but not that by the bloodvessels; hence the difference in the effect upon different substances. Potassium iodide is absorbed through the bloodvessels; its absorption is therefore not impaired by a previous injection of adrenalin. On the other hand, strychnine, potassium cyanide, physostigmine, sodium indigo-sulphate, and sodium salicylate, Exner assumes, are essentially absorbed through the lymphatics. Finally, in a few incomplete and unconvincing experiments Exner found that the absorption of toxins (abrin) is not influenced by a previous intraperitoneal injection of adrenalin, but that such an injection retards the absorption of bacteria (*proteus vulgaris*!) into the blood.

In a second communication Exner<sup>1</sup> found that with a single exception intraperitoneal injections of adrenalin did not retard the toxic effect of strychnine when the latter was injected subcutaneously. The intraperitoneal injection of adrenalin had, however, a distinctly retarding influence upon the effects of strychnine and physostigmine when these substances were introduced into the stomach of the animal.

In the experiments of Exner, with the exception of iodide of potassium, the absorption of all substances from the peritoneal cavity was retarded by a previous intraperitoneal injection of adrenalin. Such an injection, however, did not affect the absorption of strychnine when administered subcutaneously. So far these observations coincide with our experience with frogs, namely, that a retardation occurs when both substances come in contact, but not when they are injected in separate localities. But Exner's experience with the absorption from the stomach would seem to demonstrate that the (non-intravenous) application of suprarenal extract in one place is capable also of retarding the absorption from

<sup>1</sup> Arch. f. experim. Pathol. u. Pharmakologie, 1903, Bd. 1. p. 313.

another place. An analysis of Exner's observations will show, however, that they permit an entirely different interpretation than the one given to them by Exner. The fact that the intoxication with strychnine, for instance, appeared so much later in the adrenalized animals was taken by Exner to show that the absorption from the stomach was retarded. In a series of experiments published some years ago by one of us it was clearly demonstrated that strychnine is not absorbed within the rabbit's stomach<sup>1</sup> and is very little absorbed in the stomach of the dog.<sup>2</sup> This has since been repeatedly confirmed. The toxic effect of strychnine when introduced into the stomach is due to its transportation into the intestines, where it is rapidly absorbed. When the movements of the stomach are impaired, for instance, after cutting the vagi, the toxic effect is considerably retarded, due to a retardation in the removal of the strychnine from the stomach into the intestines. Now, according to Langley,<sup>3</sup> the extract of suprarenal bodies causes inhibition of the movements of the stomach. Therefore we may justly assume that the retardation of the toxic effect of the strychnine introduced into the stomach, which Exner observed, was not due to an impairment of the absorbing power of the stomach, but to an inhibition of the movements of this organ. The theory of Exner that adrenalin affects the absorption by the lymphatics and not that by the blood-vessels we shall discuss later.

In our experiments on frogs and practically also in the experiments of Exner, the delaying effect of suprarenal extract was observed only when the toxic or other substances were applied to the same tissues to which previously the extract was applied. When the two substances were incorporated in different parts of the body the delaying effect was not demonstrable. (Exner's observations on the intragastric application of strychnine, etc., are no exception, since they permit, as stated above, another interpretation.) This fact is very well compatible with the theory that the delaying effect of adrenalin is due to an impairment of the powers of absorption of the tissues. The tissues to which suprarenal extract is directly applied receive a dose of this substance sufficient to affect them profoundly in some way, so as to render them unable to absorb, to carry into the circulation, any substance with which they subsequently come into contact. Other tissues of the animal body, however, will be affected by the application of the extract to a distant part only by so much as would be absorbed into the blood and carried to them. The amount of extract which these tissues will thus receive will be very minute and could hardly exert a perceptible effect. We should also bear in mind that if the direct contact with suprarenal extract impairs the absorption, the extract itself when injected intra-

<sup>1</sup> S. J. Meltzer, *Journal of Experimental Medicine*, 1895.

<sup>2</sup> S. J. Meltzer, *THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES*, November, 1899.

<sup>3</sup> *Journal of Physiology*, 1901-1902, vol. xxvii. p. 237.

peritoneally or subcutaneously would be prevented from being completely absorbed. Under these circumstances the proper method of studying the effect of suprarenal extract upon absorption appears to be by intravenous application. This method was employed by us in most of our further experiments which we carried out mostly on rabbits, the adrenalin being injected into the ear veins.

We shall report first our experiments with strychnine. An abbreviated protocol will illustrate our results.

*Experiment 2.* Rabbit 1, control, 1625 grams, received subcutaneously strychnine nitrate 0.505 mgm. per kilo. After thirteen minutes characteristic tetanus. Survives.

Rabbit 2, 2000 grams; 1 c.c. adrenalin into the ear vein; three minutes later subcutaneous injection of strychnine 0.55 mgm. per kilo. Watched for three hours; animal somewhat prostrated, no spasms, no reaction even after handling.

The difference between the two animals in this experiment is quite striking. While the control with 0.505 mgm. strychnine per kilo had a tetanus after thirteen minutes, there was no reaction in the adrenalin animal, though the dose of strychnine was even larger—0.55 per kilo.

The experiments have shown clearly that an intravenous injection of a comparatively moderate dose of suprarenal extract is capable either of completely overcoming or distinctly delaying and greatly mitigating the effects of a surely fatal dose of strychnine. For the mitigating effect of the extract it is not necessary to apply it directly to the tissues; it is sufficient if a comparatively moderate dose is brought to the tissues through the circulation. In fact, this mode of administration is much more effective; for neither in our experiments on the frogs nor in the experiments of Exner on rabbits and guinea-pigs did the hypodermic or the intraperitoneal injection bring out such striking results as we obtained by the intravenous method.

For the continuation of our studies we deemed it advisable to study the effect of suprarenal extract upon the absorption of a substance which gives characteristic signs, but which is otherwise innocuous to the tissues and functions of the animal body. Such a substance we found in fluorescein. It stains the skin and mucous membranes yellow, also the fluids and tissues of the body (except the nervous system), but is otherwise perfectly harmless.

Fluorescein is the mother-substance of eosin. It is slightly acid and gives with alkalies easily soluble salts. In concentrated solutions it is dark red without fluorescence. When diluted it is at first yellowish-red, and in still further dilution it becomes yellow and shows a brilliant yellowish-green fluorescence. The fluorescence is still recognizable in a dilution of 1:2,000,000 (Ehrlich). Our first experiments were made with the stain kindly given to us by

Professor Ehrlich,<sup>1</sup> probably a potassium salt. For the further experiments the salt was prepared by the addition of sodium hydrate to Gruebler's fluorescein.

The several series of experiments, the results of which we will now report, were carried out by subcutaneous and intravenous injections of that substance.

In the first series of experiments the suprarenal extract as well as the fluorescein were administered by subcutaneous injection in different parts of the body. We shall illustrate the results again by one protocol.

*Experiment 3.* Rabbit 1, brown; subcutaneous injection of adrenalin 2 c.c. Eleven minutes later injected into the opposite side 20 c.c. 5 per cent. fluorescein. Twenty-one minutes after last injection conjunctivæ, gums, and ears yellow; forty-two minutes after injection appearance of Ehrlich's line; later the entire pupil greenish.

Rabbit 2, brown, control; injected subcutaneously 20 c.c. 5 per cent. fluorescein. After eight minutes ears, gums, conjunctivæ yellow; five minutes later all very yellow; twenty minutes after injection distinct Ehrlich's line and the entire pupil greenish.

The yellow color of the skin and mucous membrane as well as the greenish color of the pupils was more intense in the control than in the adrenalin animal.

The delay which occurred when suprarenal extract was administered subcutaneously was, however, variable in degree and never so pronounced as in some cases when it was administered intravenously, when the delay amounted to nearly a complete suppression of the signs. The following experiment is a good illustration.

*Experiment 4.* Rabbit 1, large, brown; injected subcutaneously 5 c.c. of 5 per cent. fluorescein. Conjunctivæ and ears yellow after ten minutes; gums, skin of neck and anus after fifteen minutes; pupil greenish after thirty-five minutes; Ehrlich's line after forty minutes.

Rabbit 2, brown; injected subcutaneously 2 c.c. of adrenalin; two minutes later injected subcutaneously in other side 5 c.c. of 5 per cent. fluorescein. Conjunctivæ yellow (very faint) twelve minutes after last injection; gums twenty-five, anus twenty-seven, skin of neck thirty, ears thirty-three, Ehrlich's line thirty-three, and pupils greenish thirty-eight minutes after injection of fluorescein.

Rabbit 3, large, black; injected into ear vein 1 c.c. of adrenalin.

<sup>1</sup> In fact the stimulus to the entire work was given by an observation made September, 1903, in Ehrlich's Institute for Experimental Therapeutics, Frankfurt. Professor Ehrlich wished to show the well-known line on the cornea brought out by a subcutaneous injection of fluorescein into a rabbit. The experiment failed; the rabbit, which received a large dose of the stain, did not even become yellow. One-half hour previous to this experiment I had injected intravenously into the same rabbit a large dose of adrenalin for the purpose of bringing out the effect of the removal of the superior cervical ganglion upon the pupil. It was then that the suggestion occurred to me that suprarenal extract possibly affects absorption.—S. J. M.

Three minutes later injected subcutaneously 5 c.c. of 5 per cent. fluorescein; twenty-seven minutes after last injection ears yellow (very faintly); eighty-eight minutes later conjunctivæ, gums, and anus very faintly yellow; skin of neck very faintly yellow after two hours. Ehrlich's line and greenish pupils never appeared.

While there was also a moderate delay in rabbit 2 (extract subcutaneously) there was nearly a complete suppression of any effect from 5 c.c. of 5 per cent. fluorescein in the animal which received suprarenal extract into the ear vein.

However, even with intravenous administration of suprarenal extract the result was not always so striking as in the foregoing experiment.

This series of experiments then brought out the following results: A subcutaneous injection of a large dose of adrenalin (2 c.c.) retards and diminishes the coloring of skin and mucous membranes due to a subsequent subcutaneous injection of fluorescein. The retarding effect is much stronger when the suprarenal extract is injected intravenously, the result being sometimes nearly equal to a complete suppression of the appearance of the color. The degree of the retarding influence, however, is variable and for the present, at least, nothing can be stated as regards the cause of this variability.

All the experiments hitherto recorded agree in the general result that a previous administration of suprarenal extract retards the appearance and reduces the intensity of the effects of a substance subsequently injected subcutaneously. This retardation and mitigation can hardly be due to a chemical interaction between the extract and the other substances, since the effect is the same, in rabbits at least, whether suprarenal extract and the other substance come into direct contact or are injected into different parts of the body. Neither could it be due to some biological neutralization, since even the appearance of the color of such an innocuous substance as fluorescein is retarded by a previous administration of suprarenal extract.

We have, then, to assume that the retardation might be due to some impairment in the mechanism of absorption. We have to remember, however, that in the chain of events between the injection of strychnine and the occurrence of convulsions, or between the injection of fluorescein and the appearance of the color in the skin and mucous membranes, these substances, besides their absorption into the blood, have to be transuded into the lymph again and then taken up by the different tissue cells before the signs or symptoms can make their appearance. Now the retardation might be due, not to a slowing of absorption, but to some disturbance in some other part of that chain, for instance, to a disturbance in the lymph secretion. Or the retardation might be due even to greater elimination by the specific organs, as the liver or



kidneys, thus preventing the rapid accumulation of the necessary minimum dose within the blood. We might call to mind here that according to Langley<sup>1</sup> the injection of suprarenal extract causes indeed some increase in the secretion of bile.

To throw better light upon the questions raised here we have carried out a series of experiments in which, in the first place, the question of absorption was studied more directly by the following method: A cannula was inserted into the carotid artery, some blood was taken regularly every two, three, or more minutes into small test-tubes and permitted to clot and separate the serum. When a sufficient quantity of fluorescein was injected subcutaneously, the serum showed a distinct fluorescence varying in degree according to the quantity and according to the interval after the injection. In the first period after an injection the fluorescence of the serum is the stronger the later the blood is taken; in the second period it is the reverse; the later the blood is taken the less fluorescence is present. Suprarenal extract causes rapid clotting of the blood, and it was more convenient to obtain the blood directly from the artery, since the cannula frequently became obstructed by clots. We shall now again illustrate our results by one greatly abbreviated protocol.

*Experiment 5.* Rabbit 1, brown, 1500, morphine subcutaneously, cannula in carotid artery; adrenalin 1 c.c. into ear vein; eleven minutes later 1 c.c. adrenalin subcutaneously; five minutes later injected subcutaneously 1.5 c.c. 5 per cent. fluorescein. Blood taken first every minute, then every two minutes.

Rabbit 2, brown, 1500, morphine, cannula in carotid; injected subcutaneously 1.5 c.c. 5 per cent. fluorescein; blood taken as above.

Serum of the tubes from both animals compared. In control, fluorescence after one minute; in adrenalin after two minutes, distinctly fainter. Fluorescence of serum taken from adrenalin animal after eleven minutes not perceptibly stronger than that of the serum from the control taken one minute after the injection of fluorescein.

In a few experiments in which at the beginning there was distinctly less fluorescence in the serum of the adrenalin animal the relation soon became reversed, so that about twenty minutes after injection there commenced to be more fluorescence in the serum of the adrenalin animal than in the control. The reason for it apparently was, that while in the control the absorption of the greatest part of the injected fluorescein took place in the first few minutes and the accumulated coloring substance within the blood began to disappear by transudation and elimination, both these processes, absorption and elimination, were delayed in the adrenalin

<sup>1</sup> Loc. cit.

animal while the fluorescein continued to be slowly absorbed, thus gradually increasing the amount of the coloring matter within the blood, since its elimination from the blood was also delayed.

In order to rule out at least one of these factors, the continuation of absorption, in a few experiments the injections were made into one of the hind legs and some time after the injection the legs were tightly constricted above the injected stain, thus preventing further absorption. The following protocol is an example of such an experiment:

*Experiment 6.* Rabbit 1, black, very young, 900, morphine, carotid artery,  $\frac{1}{2}$  c.c. adrenalin into ear vein; two minutes later  $\frac{1}{2}$  c.c. 2 per cent. fluorescein into right hind leg . . . blood regularly taken. . . . Ten minutes after injection of fluorescein leg ligated above site of injection; animal killed half-hour after injection.

Rabbit 2, black, very young, 900, morphine, carotid artery; injected  $\frac{1}{2}$  c.c. 2 per cent. fluorescein into the right hind leg; blood regularly taken; ten minutes after injection leg ligated above site of injection. Animal killed half-hour after injection.

In these animals there was no further absorption ten minutes after injection. The blood specimen of the adrenalin animal taken twenty-nine minutes after injection of fluorescein showed less fluorescence than the specimen from the control animal taken four minutes after injection.

By this series of experiments, then, it was established beyond a doubt that an intravenous injection of suprarenal extract retards in a greater or less degree the absorption into the blood of fluorescein administered by subcutaneous injection. We should add that in these experiments, too, the degree of impairment of absorption varied in individual animals.

In our studies on the blood of adrenalin animals we made a few minor observations which we might mention here briefly. In the first place we can confirm the statement of Vosburgh and Richards<sup>1</sup> that the blood of adrenalin animals clots more readily than that of the controls. We noted, however, that the clots of these animals contracted a good deal more slowly, and the serum separated a good deal later than in the controls. It was also noted that the blood of adrenalin rabbits manifested a greater inclination to hæmolysis than the blood of their normal mates.

We have then established that suprarenal extract impairs in some way the absorption from the tissues. What structures become affected? Exner assumes that it is the absorption by the lymphatics which becomes impaired. He bases this assumption on his experiment in which the absorption of an emulsion of paraffin was somewhat impaired after a preceding intraperitoneal injection of adrenalin. Such an experiment, however, justifies only the conclusion that

<sup>1</sup> American Journal of Physiology, 1903, vol. xi. p. 30.

the lymphatics are impaired also, but not that the absorption by the bloodvessels is unaffected.

In our experiments with fluorescein we have repeatedly established that already one minute after a subcutaneous injection there was a definite fluorescence in the serum of the blood. Such a very rapid absorption into the blood could impossibly take place through the lymphatics. We take, therefore, the stand that suprarenal extract affects in some way the absorption through the bloodvessels, and, judging by the experiments of Exner, probably also the absorption through the lymphatics.

What is the influence of suprarenal extract upon elimination from the blood? It was mentioned above that in some experiments there seemed to be at a certain period more fluorescence in the blood of the adrenalin animal than in that of the control. The conclusion was unavoidable that in these cases there has been in the adrenalin animal a delay in the elimination of the absorbed coloring matter. Similar observations were made when the color of the skin, mucous membranes, etc., was taken as an indication of the presence of fluorescein in the animal body. It was sometimes observed that the adrenalin animal was still yellow, while the control had lost all traces of the stain.

To study the elimination from the blood it was necessary to have the adrenalin animal and the control on the same footing as regards absorption. We have therefore carried out a series of experiments on rabbits in which the fluorescein also was administered intravenously, and either the time of the disappearance of the color from the skin, etc., was studied, or the sera of both animals were compared as regards the degree of their fluorescence. Many experiments had to be made in this series before we could obtain satisfactory results. The injected quantity of fluorescein was either too large or too small; in either case the differences were not sufficiently striking.<sup>1</sup> We had, however, quite a number of successful experiments which left no doubt that the elimination of fluorescein from the blood was in a greater or less degree retarded in the adrenalin animal. The following examples will illustrate it:

*Experiment 7.* Rabbits 1, 2, and 3; gray, 1000 grams each; received into right ear veins 0.5 c.c. adrenalin, and seventeen minutes later 1 c.c. of 5 per cent. fluorescein into the left ear veins. Rabbit 4, gray, control, 1000 grams; received into the ear vein 1 c.c. of 5 per cent. fluorescein . . . . at first control more yellow all over. . . . Two hours later adrenalin animals showed more yellow color than the control. One adrenalin animal died. . . . Two hours and forty minutes after injection blood taken from two adrenalin animals and from the control.

<sup>1</sup> By accident we had, at the time we were carrying out this series, only young, small rabbits at our disposal. Only small doses of adrenalin could be administered, and that only in fractions; and even so we lost many animals from pulmonary oedema.

Serum of control definitely less fluorescent than that of adrenalin animals.

The series of experiments in which the fluorescein was injected intravenously, definitely brought out the fact that in the adrenalin animal the color disappears from the blood much later than in the control. The same is true also of the color of the skin and mucous membranes; it disappears later in the adrenalin animal. However, it was also seen that after there was no more color in the skin, etc., in either of the animals, there was still fluorescence in the blood of both animals, but again more in the adrenalin animals.

We may add that in intravenous injection of fluorescein there was in the adrenalin animal at first a distinct retardation in the appearance of the color in the mucous membranes and especially in the skin. We can interpret this only by assuming that there was a retardation either in the secretion of the lymph or in the taking up of the color by the tissue cells or in both processes.

The delayed elimination of any substance from the blood may be due to a retardation in the elimination of this substance by the kidneys, the liver, or both, and to a degree also to a delay in the reabsorption of the substance from the tissues and the lymph. That the reabsorption is indeed delayed would seem to be supported by the fact that the coloration of skin and mucous membranes persists perceptibly longer in animals which received an intravenous injection of adrenalin. We have not, however, studied this problem by direct experiments.

The question of retardation of elimination by the kidneys and the liver we have already studied in numerous experiments. But we are not yet ready to report our results in this paper. The conditions are quite complicated and a good deal more experimentation will have to be done before definite statements can be made. Especially is the frequent pathological condition of the kidneys in apparently normal animals quite a disturbing factor in the study of that problem. We had, for instance, animals in which the kidneys of the adrenalin individual were perfectly green (fluorescein), while that of the control showed no staining at all—on account of the fatty degeneration of the kidneys of the control animal. We hope, however, in the near future to be able to offer some positive results in regard to that vexed problem.

A subject of greater concern to us was the question whether the normal transudation from the blood into the surrounding tissue spaces, the formation of lymph, is affected by the administration of suprarenal extract. We have already stated above that even in the intravenous application of fluorescein the coloring of the skin and mucous membranes was perceptibly retarded by a previous administration of the extract, which can mean only that the passage of the stain from the blood into the tissues occurred with less freedom than in normal animals. However, the chief obstacle might

have been not in the stain traversing the capillary wall, but in its reaching the cells, the "absorption" into the epithelia.

Our attempt to study directly the appearance of the stain in the lymphatics of the mesentery was not very successful; we were not sure enough that the lymphatics in the adrenalin animal show the stain later than those of the control.

The following method, however, brought satisfactory evidence that also the transudation through the capillaries is notably affected by an administration of suprarenal extract. The animals received intraperitoneal injections of sodium chloride (0.9 per cent.), and then every few minutes small quantities of it were withdrawn and tested for the presence of fluorescence. The following abbreviated protocols of such experiments will illustrate our results:

*Experiment 8.* Rabbit 1, white, 1000 grams; ether; 0.6 adrenalin into right ear vein; twelve minutes later 25 c.c. salt solution into peritoneal cavity, and two minutes after  $\frac{1}{2}$  c.c. of 2 per cent. fluorescein into left ear vein; test fluid regularly taken from peritoneal cavity.

Rabbit 2, white, 1000 grams; ether; 25 c.c. salt solution into peritoneal cavity, and one minute later  $\frac{1}{2}$  c.c. 2 per cent. fluorescein into ear vein; tests regularly taken.

Result: Solution taken from the peritoneal cavity of adrenalin animal twenty-one minutes after injection of fluorescein is not as fluorescent as the solution taken from the control eight minutes after the injection.

In order to increase the transudation of fluorescein and also to exclude the threatening factor of nephritis in one of the animals, some experiments were carried out on previously nephrectomized animals.

*Experiment 9.* Rabbit 1, white, 1000 grams; ether; vessels of both kidneys ligated through lumbar incision; 0.5 c.c. adrenalin into right ear vein; eight minutes later 0.4 adrenalin intramuscularly, 25 c.c. salt solution into peritoneal cavity; three minutes after last injection of adrenalin injected into ear vein  $\frac{1}{2}$  c.c. 2 per cent. fluorescein; tests regularly taken.

Rabbit 2, 1000 grams; ether; lumbar nephrectomy; 25 c.c. salt solution into peritoneal cavity,  $\frac{1}{2}$  c.c. 2 per cent. fluorescein into ear vein; tests regularly taken.

Result: Test taken from adrenalin animal twenty minutes after injection equal in color and fluorescence to that taken from control ten minutes after injection of fluorescein.

These series of experiments left no doubt that the fluorescein transudes from the blood into the peritoneal cavity distinctly more slowly in animals which had previously received intravenous injections of suprarenal extract than in normal animals.

From our experiments it appears probable that the transudate in adrenalin animals is poorer in proteids than that of the control,

a fact which could be utilized in the study of the question of the effect of suprarenal extract upon the formation of lymph. However, in such a case the amount of the proteids present in the peritoneal fluid of each animal would have to be established before the injection of the extract—which we have not done.

It is worth recording that when the peritoneal fluid became somewhat richer in proteid content in the adrenalin animal, it became so completely clotted that the test-tube could be inverted. Suprarenal extract apparently hastens clotting even in transudates. We shall recur to it in later studies.

We shall record here an experiment reported by Wessely<sup>1</sup> a few years ago, which also demonstrates the retarding effect of suprarenal extract upon the process of transudation. He injected suprarenal extract (suprarenin, v. Fürth) into the subconjunctival tissue of one eye of a rabbit, and after fifteen minutes opened by puncture the anterior chambers of both eyes. On the normal side the anterior chamber filled up again after ten to fifteen minutes, while on the adrenalin side it did not attain its natural state even after thirty minutes. The aqueous humor on the adrenalin side was also poorer in proteids than on the normal side.

Our several series of experiments have established two essential facts: that suprarenal extract retards absorption from the tissues into the blood, and retards transudation from the blood into the tissues. In the process of transudation no other capillaries are concerned than those of the blood. We have given above our reasons for the belief that suprarenal extract affects in the first place the absorption by the bloodvessels and probably also the absorption by the lymphatics. In short, suprarenal extract affects the capillaries in such a manner that the passage of fluid through their walls in either direction is impaired, retarded.

What is the nature of this impairment? As the rise of blood pressure is the best-known property of the suprarenal extract, and as the intracapillary pressure is a more or less potent factor in the production of lymph, that is, in the processes of transudation and absorption, the suggestion presents itself that the impairment of these processes by the suprarenal extract has something to do directly with the blood pressure-raising property of the extract. A closer analysis of the concerned facts will show, however, that such an assumption is untenable.

In the first place, the rise of blood pressure could not be the cause of the retardation of the two opposing processes at the same time. For instance, if the rise of blood pressure would cause a rise of the intracapillary pressure it would indeed impair absorption, but then it should rather favor transudation. Or, if the intracapillary pressure would be diminished, as is probably the case when

<sup>1</sup> Bericht der Ophthalmologischen Gesellschaft, Heidelberg, 1900, p. 69.

the rise of blood pressure is due to a strong constriction of all the small arteries, transudation would be retarded; but then absorption would be favored instead of being impaired. Besides, in nearly all experiments the impairment of absorption and transudation through intravenous injection of adrenalin was taking effect long after the effect of the blood pressure had passed off, the rise in pressure usually only a few minutes.

Neither could the impairment be due to chemicophysical changes in the blood and lymph, since such changes again could be effective only for one of the opposing processes, but not for both at the same time and in the same manner.

The theory which we are going to offer, in explanation of retardation of absorption and transudation which is caused by the administration of suprarenal extract, consists in the assumption that the extract decreases the permeability of the endothelial wall of the capillaries, and is based upon a view of the vital nature of the changes of this permeability brought forward by one of us in another paper.<sup>1</sup> (In fact, it was this view which gave the stimulus for the present investigation.)

This view is as follows: 1. The endothelia, like all organized matter, have pores; whether these pores run in a straight line or whether the fine canals connecting both surfaces of the endothelial cells run in a tortuous course is immaterial for our purpose. 2. The endothelia are living tissues and possess irritability and contractility. We know now that they are phagocytes, which of course presupposes contractility. These two premises are generally acknowledged facts. If these premises are true, the following ought to be true also: both surfaces of the endothelia are connected by pores, each of which is surrounded by contractile tissue. But as contractile tissue is sometimes more and sometimes less tonically contracted, and the tonicity can be increased and decreased by various stimuli, we have to assume that the tissue around the pores is sometimes more, sometimes less contracted; that means that the lumina of the pores change according to the state of the tonicity of the endothelial tissue, and according to the stimulation to which it is exposed at different times. Accordingly, the endothelial pores are fine canaliculi surrounded by contractile sphincters which control the size of their lumina. In other words, the contractility of the endothelia controls their permeability. The permeability of the living vascular endothelia is therefore essentially different from the physical permeability of dead animal membranes; it is a vital phenomenon. It is obvious that no matter what other factors control transudation and absorption of lymph, the vital permeability of the vascular endothelia will influence these processes to a considerable degree. Whether the essential factor is the intra-

<sup>1</sup> S. J. Meltzer, Lectures on Edema, Harrington Lectureship, Buffalo, 1903.

capillary blood pressure (Ludwig, Starling), or the osmotic pressure within the tissue cells and the lymph spaces (v. Koranyi, J. Loeb), or some vital activity of the tissue cells (Lazarus-Barlow, Asher), or whether all these factors work together in the processes of absorption and transudation of lymph (Meltzer), the size of the lumina through which the interchange of the fluids takes place will necessarily influence the end result; and the size of the lumina depends upon a changeable, vital factor, the contractility of the endothelial cell. Whether it is necessary to assume that the endothelial wall has still another vital activity, a secretory function (Heidenhain, Hamburger), that question we shall not discuss here. We shall only point out that in contradistinction to the secretory theory of lymph, in our assumption no new "vital" property is attributed to the vascular endothelia; irritability and contractility are accorded to them by all writers.

To recapitulate briefly, the endothelial pores through which probably the exchange of fluid in the processes of transudation and absorption takes place, are surrounded by a contractile tissue which is capable of changing the lumen of these pores, thus influencing the rate of these processes.

In normal processes the degree of contractility, the tonicity of the endothelia, is determined by the metabolic processes within the endothelia themselves as well as by the nature of the substances with which they come into intimate contact, on the blood side as well as on the lymph side of the blood capillaries.

The question that presented itself to us now was whether there are not substances by means of which we can at will increase and decrease the tonicity of the endothelial protoplasm, thus increasing and decreasing the vital permeability of the endothelia and hindering or facilitating the processes of transudation and absorption. We thought of the suprarenal extract as such a substance—hence the present series of experiments.

Now we have established by these experiments that the administration of suprarenal extract indeed retards transudation as well as absorption of some foreign substances through the capillary walls. We are therefore ready to explain these retardations by the assumption that suprarenal extract increases the tonicity of the endothelial protoplasm and thus decreases the vital permeability of the vascular wall.

That the extract is capable of increasing the tonicity of contractile tissues we know from its effects upon the striated and smooth muscle fibres. Oliver and Schaefer<sup>1</sup> found that the effect of the suprarenal extract upon striated muscle is to prolong its contraction. The rise of blood pressure which is caused by the effect of the extract upon the smooth muscle fibres of the arteries lasts for many

<sup>1</sup> Journal of Physiology, 1895, vol. xviii, p. 230.



minutes, and it was shown<sup>1</sup> that the contraction of the bloodvessels of the rabbit's ear can be considerably prolonged by section of the cervical sympathetic nerve. Furthermore, the extract causes also a dilatation of the pupil, apparently by stimulating its dilator, which, according to Langley and Anderson,<sup>2</sup> is a "radial contractile substance," although, as they state, they could not satisfy themselves "that it has the form of ordinary unstriated muscular tissue." It was shown further<sup>3</sup> that when the superior cervical ganglion was removed (in rabbits and cats), the dilatation of the pupil may last a few hours. The same authors<sup>4</sup> have stated recently that in frogs subcutaneous injection or instillation of small doses of adrenalin causes normally a dilatation of the pupil which lasts more than twenty-four hours. Suprarenal extract possesses, then, the property of increasing the tonicity of contractile tissues, which effect seems to last the longer, if we may say so, the less the contractile tissue is organized. We wish to bring out this point especially on account of the popular view that the effect of suprarenal extract is only of very short duration. This view is based upon the experience with the effect of the extract upon blood pressure. In our experiments on absorption and transudation the retarding effect of suprarenal extract was present long after its injection. We do not know exactly how long the retarding effect lasts, but it certainly lasts a good deal longer than the effect upon the blood pressure. However, we doubt greatly whether it lasts as long as the effect of the extract upon the pupil, which, as stated above, may last even longer than twenty-four hours.

Our theory, then, in brief is as follows: Suprarenal extract causes an increase of the tonicity of the contractile protoplasm of the endothelia of the blood capillaries and lymphatics. This increase in tonicity narrows the lumen of the pores and decreases the facility for the interchange between the blood and the tissue fluid (lymph). In other words, the extract decreases the vital permeability of the capillary wall; hence the retardation of absorption and transudation.

The following is a brief *résumé* of our results:

1. Intravenous injections of suprarenal extract retard invariably the processes of absorption and transudation.
2. Subcutaneous injections also often show a retardation of these processes; the effect, however, is neither strong nor constant.
3. In frogs the retardation of absorption of some substances was recognizable only when suprarenal extract was previously mixed with that substance, or when both substances were injected into one and the same lymph sac.

<sup>1</sup> S. J. and Clara Meltzer, *American Journal of Physiology*, 1903, vol. ix. p. 252.

<sup>2</sup> *Journal of Physiology*, 1902, vol. xiii. p. 554.

<sup>3</sup> S. J. Meltzer and Clara Meltzer Auer. *American Journal of Physiology*, 1904, vol. xi. p. 23.

<sup>4</sup> *Ibid.*, p. 449.

4. It is assumed that the suprarenal extract increases the tonicity of the protoplasm surrounding the pores of the endothelia of the capillaries, thereby reducing the facility for the interchange between the blood and the tissue fluid.

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## A STUDY OF BRAIN TUMORS.

WITH REPORTS OF FOUR CASES.

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AND

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UNDER brain tumors are included any new-growth upon or within the substance of the brain, including cysts and aneurysms, but excluding abscess. As many as sixteen or seventeen different pathological varieties of growths have been named. Of these the most important and most frequent are gliomata, sarcomata, including endotheliomata, tubercles (tyromata), and syphilitic gummata. Among some of the less frequent are carcinomata (secondary), psammomata, cysts, and angiomatica.

As to the relative frequency of the more important varieties statistics are at variance. Starr's table of 600 cases gives: tubercles, 30 per cent.; glioma (including gliosarcoma), 20 per cent.; sarcoma, 20 per cent.; carcinoma, 8 per cent., and gumma, only 4 per cent. Another list of 100 cases gives: glioma, 20 per cent.; sarcoma, 18 per cent.; tubercles, 13 per cent., and gumma, 13 per cent., while carcinoma has 7 per cent. Of the cases herewith reported three are sarcomata and one a glioma.

There is also a decided lack of agreement as to the frequency of occurrence of brain tumors in general. In all probability intracranial tumors are considerably more frequent among the insane than in the entire population. Clouston stated that 28 per cent. of the insane have brain tumors, while Esquirol gives the frequency as low as 2.7 per cent. Blackburn<sup>1</sup> found in 1814 autopsies upon bodies of the insane dying at the Government Hospital for the Insane at Washington 31 cases with intracranial tumors, or a proportion of 1.7 per cent., or 1 case in 58.

ETIOLOGY. In general, the causation is obscure. As to age, the decade from thirty to forty years seems to have the greatest number, with a considerable predominance of cases in the years under thirty

<sup>1</sup> Intercranial Tumors among the Insane, 1903.

over those after forty, showing greater frequency in the young than in the old.

The male sex seems more subject than the female, in the proportion of 5 to 3, or 3 to 2.

A history of trauma preceding the appearance of the tumor is given in a large number of cases, but probably the importance of these injuries is somewhat overestimated. Tubercles and gummata are, of course, the result of specific infections, and carcinomata are invariably metastatic from tumors in other parts of the body.

For convenience in locating new-growths in the brain, it may be divided into a number of areas.

1. Frontal lobes.
2. Motor cortex.
3. Parietal region.
4. Occipital lobes.
5. Temporal lobes.
6. Corpus callosum.
7. Basal ganglia and internal capsule.
8. Corpora quadrigemina and pineal gland.
9. Pituitary body.
10. Crura cerebri.
11. Pons and medulla.
12. Cerebellum.
13. Multiple tumors.

Schuster,<sup>1</sup> in his exhaustive monograph on the *Psychical Symptoms of Brain Tumor*, has made a composite table of some thousands of cases from a number of sources, showing that of all brain tumors 21.6 per cent. occur in the cerebellum; 14.7 per cent. are multiple; 12.1 per cent. in the frontal lobes, and 12 per cent. in the motor region. The region claiming the least number is the corpus callosum, with 2.5 per cent.

**SYMPTOMS.** The symptoms of brain tumor are classed as general and focal. The general symptoms are due to intracranial pressure produced by the presence of the tumor and the increased amount of cerebrospinal fluid. These may be classed under seven heads.

1. *Headache.* Usually this is the earliest symptom, and is said to occur in over 50 per cent. of all cases. The severity of the pain is characteristic. It is lancinating or boring, and may be periodic, being absent at times. Often its location is indicative of the position of the tumor.

2. *Vertigo.* This is present in about one-half of the cases, and is often so severe that the patient may fall. It is most frequent in tumors of the cerebellum.

3. *Vomiting* occurs without reference to taking of food, without nausea or pain, and is usually of a projectile character. In one of

<sup>1</sup> *Psychische Störungen bei Hirntumoren*, Stuttgart, 1902.

the cases reported herewith vomiting occurred most frequently in the morning before rising from bed. It is present in more than 50 per cent. of the cases.

4. *Optic neuritis* and blindness is present in from 60 to 80 per cent. of all cases, and may be an early or a late symptom, but it is one of the most important signs. In our four cases it was present in three, and possibly absent in one.

5. *Mental or psychic symptoms* are said to be present in nearly all cases, but Gianelli concludes from a list of about 700 cases that definite psychical disturbances are present in about 58 per cent. of cases. In 775 cases collected by Schuster, 352 are described as having definite psychical symptoms, while the remaining 423 cases had simple mental weakness, dementia, or somnolence.

One might also say that the definite psychical disturbances are focal symptoms rather than general, as they greatly predominate in cases with tumors in certain regions, particularly the frontal lobes. While of all tumors of the brain about 22 per cent. occur in the cerebellum and 12 per cent. in the frontal region, among those tumors in which definite psychoses are present, 21 per cent. occur in the frontal lobes and only 10 per cent. in the cerebellum; or, in other words, 79 per cent. of all frontal lobe tumors are associated with psychical disturbances and 35 per cent. of cerebellar tumors. The temporal lobes also bear a close relation, as about 67 per cent. of all temporal lobe tumors have these symptoms. This predominance of frontal lobe tumors, where mental disturbances are prominent, is of interest in connection with one of our cases.

Some of the more definite mental symptoms are: 1. Epileptiform mania. 2. Melancholia and depression. 3. Confusion and hallucinations. 4. Mania. 5. Chronic paranoia. 6. Convulsions, either general or local (Jacksonian epilepsy), or both appear in 25 per cent. of all cases. Local convulsions are, of course, particularly frequent in lesions of the motor cortex, and in those cases would be a focal symptom rather than general.

6. *Constitutional disturbances*, anorexia, abnormally increased appetite, thirst, febrile movements, emaciation, disturbance of pulse (slow and irregular), and respiration are present in many cases.

7. *Focal symptoms* are said to be of two kinds: direct or destructive, those which are due to the destruction of tissue by the tumor itself, and indirect, or those caused by the pressure of the tumor upon the immediately surrounding structure of the brain.

The focal or localizing symptoms vary with the position of the tumor, and it is upon this that the diagnosis of the location of the new-growth is based. The diagnosis of the presence of a tumor is made on the presence of all or a part of the typical general symptoms as named above and such focal symptoms as may be present. These last, however, may be entirely absent.

The focal symptoms which are absolutely diagnostic are:

1. Paralysis or spasm—motor area, or possibly subcortical, affecting motor fibres (Spiller).<sup>1</sup>

2. Motor or sensory aphasia—Broca's area, or cortical centre of sight in occipital lobe, or of hearing in left temporal lobe.

3. Hemianopsia—occipital lobe or optic tract.

4. Cerebellar staggering (ataxia)—cerebellum.

Those which are helpful, but more or less doubtful, are:

1. Loss of sense of position and stereognosis—parietal region (Spiller).<sup>2</sup>

2. Definite mental changes (psychosis)—prefrontal area.

CASE I. *A round-celled sarcoma of right frontal region, apparently originating in wall of anterior horn of lateral ventricle.*—C. T., male, aged four and one-half years. In June, 1902, he had attacks of severe headache, appearing at irregular intervals, often several times a day. During such attacks he would scream and place his hands to his head. After the paroxysm of pain he would be drowsy and sleep for one or two hours. After a few weeks these symptoms disappeared, and he appeared to be quite well until December, 1902, when he had a short febrile attack which was called "la grippe." At about this time his headaches reappeared, and in addition he began to have attacks of vertigo, which were so severe that at times he would fall. He also began to vomit frequently, especially in the early morning before arising and before and after breakfast, the attacks seeming to have little relation to the taking of food. The vomiting, however, appeared to be preceded by some nausea, and the headaches were often apparently relieved by it. At this time he developed an almost insatiable appetite, and was never satisfied. All of these symptoms were increasing in severity. The writer was called February 4, 1903.

*Examination.* Appearance anæmic. No emaciation. Circumference of head,  $21\frac{1}{4}$  inches. (A sister two years older measured  $20\frac{1}{2}$  inches.) The head looks large. No areas of tenderness on percussion. Headache in frontal region. Pulse irregular. Rate, 82. Marked difference in pulse rate during inspiration and expiration. Very perceptibly quickened during inspiration. (At times later, when he was feeling fairly well, the pulse was 95 and very regular in rate.) Tongue, when protruded, always deviates to the right, but can be moved to either side. Eyes: Fundus normal. No abnormalities found upon examination by Dr. Byington. Pupils have normal reaction. Knee-jerks and other tendon reflexes normal. No ankle clonus. Skin very dry and somewhat scaly. Temperature normal.

As some gastric disorder was suspected by two consultants, a chemical examination of the vomitus was made, showing: Free

<sup>1</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, February, 1904.

<sup>2</sup> Ibid.

HCl, 0.072 gram per 100 c.c. Total acidity, 0.108 gram per 100 c.c.

On the morning of February 10th, at about 3 o'clock, the patient had a convulsive attack lasting about ten minutes. During the attack he was unconscious, and his hand was burned severely by a hot-water bottle. This convulsion was preceded by much tossing and muscular twitchings during the night. About an hour later he had another similar attack, but lighter, which began by spasmodic contractions of the motoroculi muscles (nystagmus). The pupils were widely dilated, and the eyes drawn strongly to the right and upward during the seizure. The body and limbs were rigid, and a few tonic contractions of the limbs were noted. This was followed by a period of drowsiness, and after a few days he seemed much better, but remained in bed.

He soon developed a great thirst, accompanied by marked polyuria. On February 22d a urinary test showed a quantity of 900 c.c. for six hours, with a specific gravity of 1003, and on February 26th 1500 c.c. for eight hours, with a specific gravity of 1002. He urinated very frequently. A blood test at this time showed the blood about normal, with leukocytes rather below than above normal (85 per cent.). During the time when thirst was so excessive his appetite was poor and he ate very little. In the two weeks following his first convulsive attacks he has had two or three of a similar nature.

*March 3, 1903.* In the last few days patient sleeps much, and is rather restless and stupid. He takes very little food or water. Feces and urine pass involuntarily. Now lies much on the back of his head, while before he would lie only on side or face. During the past month during my attendance very marked changes in mentality and disposition have been noticed, which are rapidly increasing in intensity. In place of a cheerful and pleasant disposition he has become irritable and cross, and shows a tendency to use vulgar language and to apply low epithets to members of the family, etc. Shows signs of mental deterioration and loss of memory. Repeats the same statement many times in an hour, and repeatedly calls for objects which have already been given him.

*May 15th.* Contractures and tetanic spasms of skeletal muscles, especially of the limbs, are gradually developing. There are no localized convulsions or contractures. The arms are completely and strongly extended, while the hands and fingers are flexed. The legs and feet are strongly extended. For the last few days his temperature has been observed to be abnormal, in the evening reaching 104°, in the morning subnormal, 96.5°.

*25th.* Patient is unable to see, and seems totally blind. His emaciation is extreme, having gradually progressed during the last three months.

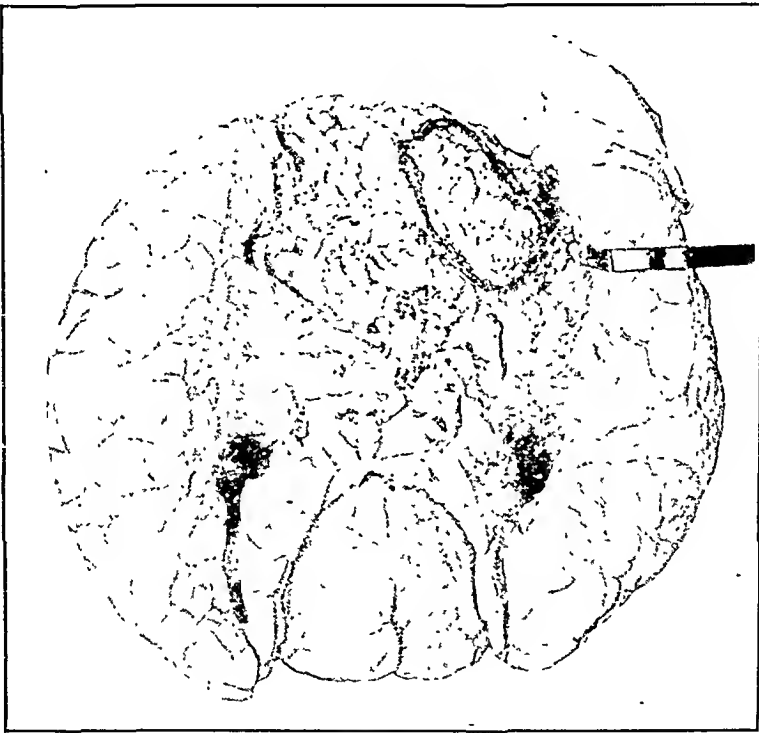
*June 3d.* Dr. Byington made ophthalmoscopic examination of eye-grounds, revealing choked disk in both eyes.

5th. While palpating scalp a marked swelling in the right frontal region was noted, soft, and about two by one and one-half inches in diameter and raised one-quarter inch above general surface of cranium.

During the past five weeks he has eaten practically nothing. The spasm of the limbs gradually became more marked. Death occurred June 9, 1903.

An *autopsy* was held five hours after death, only the cranium being opened. Head measured twenty-one inches in circumference after death. On removal of scalp the swelling mentioned in

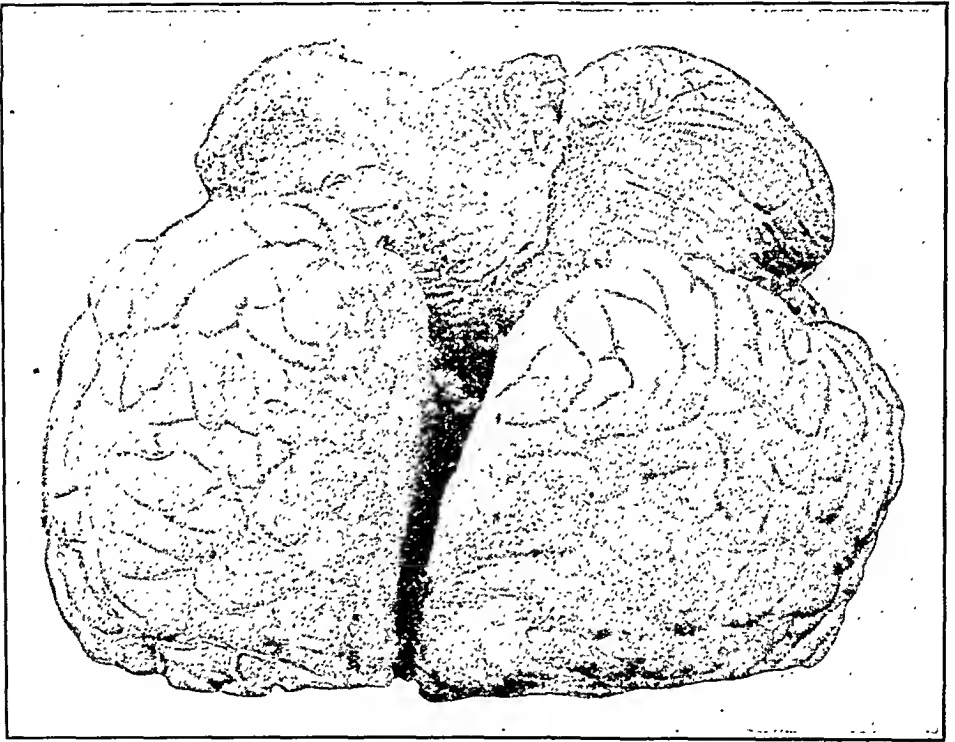
FIG. 1.



this history was found in the right frontal region. The periosteum was elevated one-fourth of an inch by a soft mass two by one and one-half inches. On removal of the periosteum it was seen to contain a pultaceous mass and puriform fluid, and the outer surface of the cranial bone was eroded and greatly roughened, but there was no visible connection with the cranial contents. The ventricles were greatly distended with a dark-colored puriform material containing numerous small masses of yellowish color, resembling the sand-like particles from an actinomycosis abscess. The brain substance was greatly thinned and the convolutions flattened. A soft yellowish granular mass was easily detached from the inner wall of the anterior horn of the right lateral ventricle, corresponding to

the area of the cortex over which the dura mater was inseparably adherent to the substance of the brain. (See Fig. 1.) This area was confined to the right frontal lobe, was two inches in diameter anteroposteriorly, and involved the first and second frontal convolutions, its posterior margin lying just at the fissure separating these from the ascending frontal convolution, also involving part of the prefrontal region. The dura mater at this area was quite firmly adherent to the frontal bone, but could be separated. The ventricular walls were softened and infiltrated with tumor cells. The optic nerves were degenerated.

FIG. 2.



CASE II. *Cyst of right cerebellar hemisphere.*—J. G., male, aged twenty-nine years. There is no history of any symptoms referable to intracranial tumor until six weeks before the death of the patient. At that time he had what was called a "bilious attack," with symptoms of nausea, vomiting, headache, and rise of temperature. Vertigo also rapidly developed.

Two weeks after the beginning of these symptoms they became so severe that he was confined to his bed, where he vomited very frequently, and loss of flesh was rapid. Two days before his death Dr. Riley was called in consultation, and found the following condition:

Dr. Riley's examination: Patient greatly emaciated, mind



stuporous, face cyanotic, both pupils dilated, severe headache at back of head, vomiting at frequent intervals.

Dr. Byington was called on the same day, and made an ophthalmoscopic examination of the eye-grounds, finding a condition of choked disk and distinct retinitis. An ophthalmoscopic examination made a few days after the onset of his first symptoms showed no changes in the retina. At that time headache was present, and Dr. Byington noted a bewildered expression of the countenance.

*Autopsy Report.* The right cerebellar hemisphere contained a cystic cavity filled with a gelatinous fluid, three-fourths inch in vertical diameter by one inch in anteroposterior and lateral diameters. It was within the substance of the hemisphere and in close contact with the basilar surface. (Fig. 2.)

*Microscopic Examination.* Round-celled sarcoma, very vascular, surrounding the cavity containing a mucoid material.

Optic nerves degenerated.

CASE III. *Sarcoma of choroid plexus, corpora quadrigemina, and pineal gland.*—A. B., male, aged twenty-eight years. The first symptom present in this case was headache, which was severe and located on the right side of the head. These pains were periodical, lasting from 3 o'clock until noon on the days when present. From two months after the beginning of this symptom until the time of his death the patient was confined to his bed. His principal symptoms at this time were progressive weakness, anorexia, and slight rise of temperature. About six weeks before the time of death the patient was totally blind. There is no record of an ophthalmoscopic examination. Two weeks before death a complete aphasia developed. The entire course of his disease was about one year.

*Post-mortem Examination.* A distinct condition of internal hydrocephalus was present. The brain was removed and three ounces of clear fluid escaped from the floor of the third ventricle. In the region of the choroid plexus, the corpora quadrigemina, and the pineal gland, so that these structures were incorporated in the mass and indistinguishable, was a tumor in size about one inch in diameter and half an inch in thickness. (Fig. 3.)

Microscopic examination shows a very cellular tumor, composed of very large round cells with distinct vesicular nuclei, and among these a large number of very small, dark-staining, round cells, resembling a small round-celled infiltration. (Fig. 4.) The histogenesis of this tumor is somewhat obscure in my mind. It appears to me as very possible, and the change in the surrounding choroid reinforces this view, that the tumor cells have their origin from the ependyma cells of the choroid plexus.

CASE IV. *Glioma of right temporal lobe.*—Miss C., aged thirty-three years. This patient was first seen by the writer about one hour before death occurred, and previous to this time her symptoms had not been of such a nature as to bring her under the care of a

FIG. 3

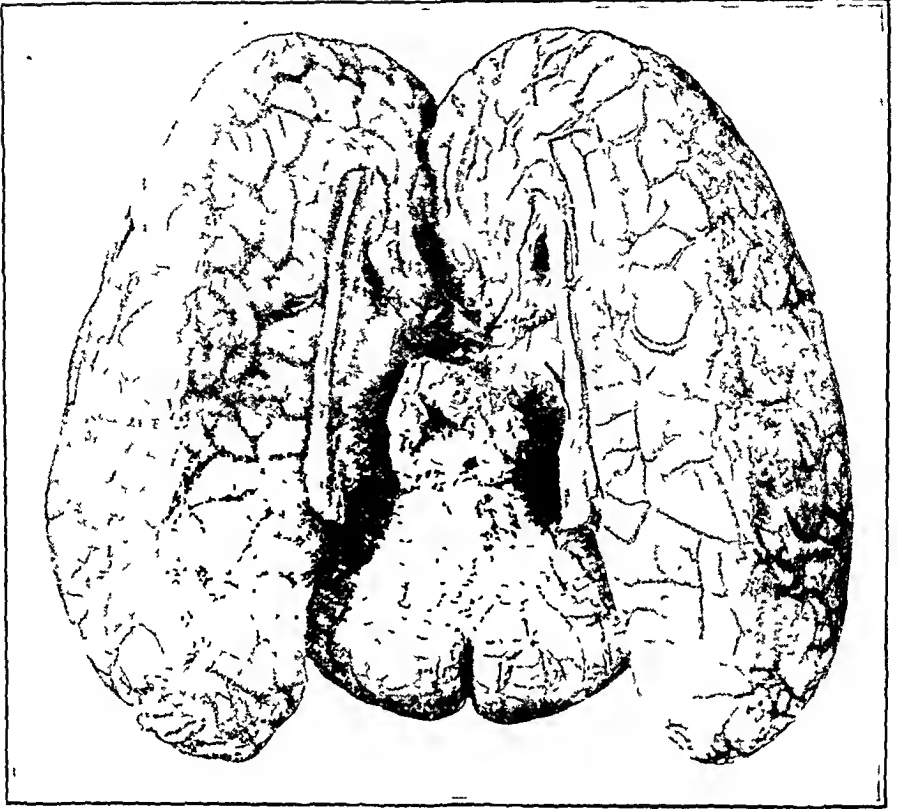
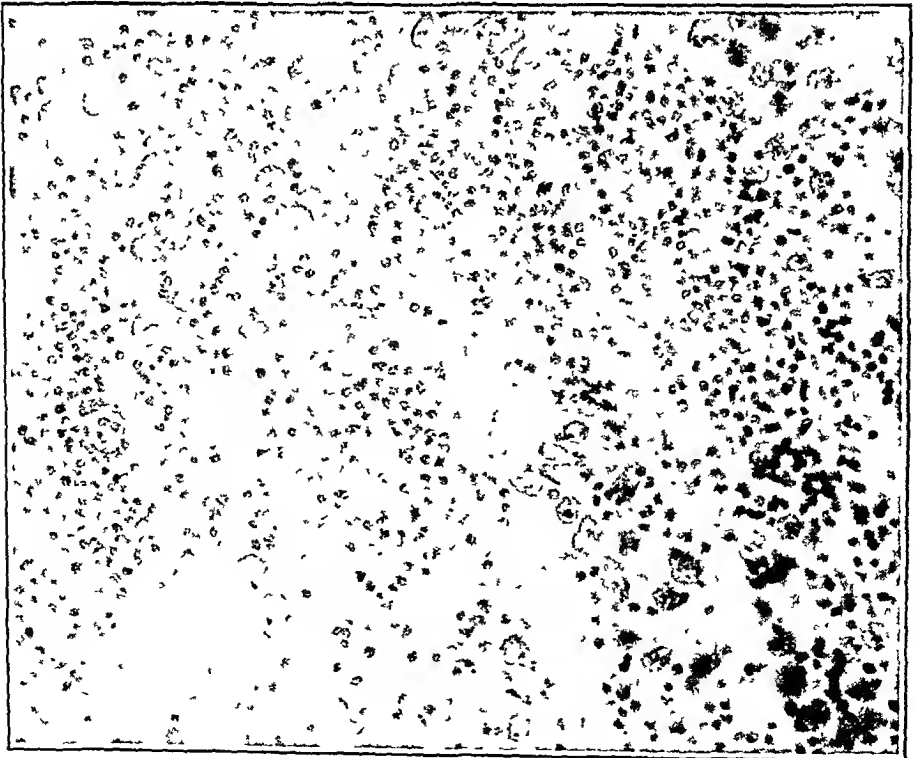


FIG. 4



physician sufficiently for a diagnosis to be made. The following history of her illness, however, was obtained:

When twenty-one years of age patient had hip-joint disease and was confined to bed. The result was complete ankylosis. She has had for three years what were called sinking spells several times in a day. On two different occasions periods of unconsciousness were experienced. During this time she had noticed frequently a tendency to pitch forward while bending or leaning forward. She also had frequent attacks of very severe headache, the location of which was not mentioned. During these three years she had vomited only twice, so far as known, once about four weeks before death, and the second time only a few hours before her death. Somnolence was a marked and increasing symptom. She slept soundly at night and much during the daytime. Among her other symptoms she complained of constipation and cold feet. Upon examination five days before time of death pulse and temperature were normal, and she complained of severe pain in and around the right eye.

Dr. Byington made a partial examination of the eyes, but no mydriatic was used and no ophthalmoscopic examination was made. Vision was imperfect, and an appointment was made for an examination on the day after death occurred.

When the writer was called on the day of her death the patient lay unconscious, although it was stated that four hours before she was rational, and that a physician who had called had prescribed some simple treatment without suspecting any serious condition. Breathing was stertorous and of the Cheyne-Stokes type. The right pupil was widely dilated and the left contracted. The pupils, however, were variable, and at times for a few minutes seemed quite normal. The whole body was convulsed by muscular spasms, tonic and clonic. The right arm would be flexed and the left strongly extended, and in a few minutes the right extended and the left flexed. Similar changes were noted in the legs.

As death approached the breathing became slower and very irregular. The face was cyanotic. Breathing finally ceased at least five minutes before the heart action ceased. The patient apparently died of respiratory failure.

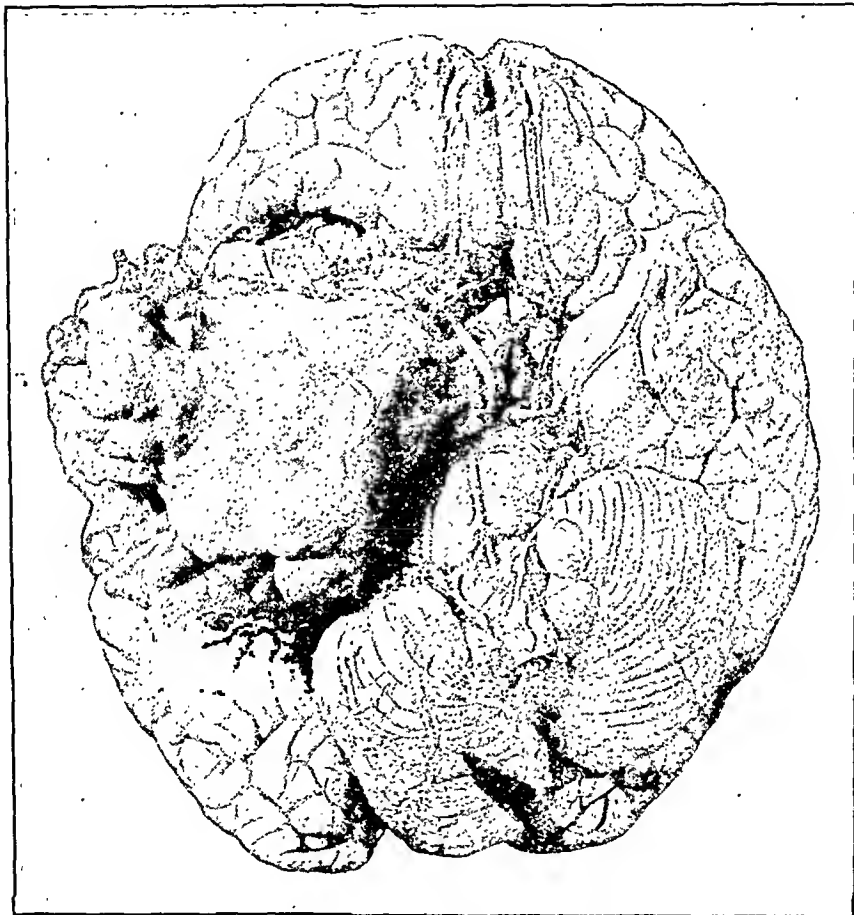
The autopsy revealed a large soft glioma of the lower surface of the right temporal lobe. At post-mortem the growth appeared pale rather than congested, and the microscopic examination revealed few bloodvessels in its structure, contrary to the usual description of such growths. There was no distinct line of demarcation between the tumor and the normal tissue. The growth in the temporal lobe had greatly displaced the cerebellum, as shown in Fig. 5.

Microscopic examination of a cross-section of the optic nerves showed a degeneration of a few fibres, but not all.

The symptomatology of these four cases, all of which were exam-

ined at autopsy, shows a striking similarity in the entire absence of all definite focal or localizing symptoms. In Case I. the body of the growth was confined to the right frontal lobe, lying just in front of but not directly affecting the motor cortex. If it had occupied a corresponding position in the left hemisphere no doubt a motor aphasia would have resulted, with agraphia if the patient had been old enough to write. The tumor in Case III. was located in the third ventricle, affecting the choroid plexus and adjacent structures.

FIG. 5.



The fact, as brought out by the patient's history, that he had been during his illness under the care of a number of physicians, including several neurologists, without a definite diagnosis, would indicate that his symptoms did not definitely point to the nature and location of the lesion. Case IV. is a third example of the same difficulty. The growth was at the base of the right temporal lobe, and there were absolutely no focal symptoms, and, indeed, a tumor was not suspected until just before death. It is possible that a similar lesion in the left temporal lobe might have resulted in word-

deafness. However, in Case I. the location of the headache in the frontal region and the definite nature of the psychic symptoms present might direct one to the frontal lobe as the seat of the lesion. The idea that the frontal or prefrontal region is one of the principal centres of memory and reasoning has support from many sources, one of which was mentioned in the discussion of symptomatology above, where attention was directed to the greater frequency of definite psychic symptoms in tumors of the frontal lobe than in those occurring in any other portion of the brain. Mynert,<sup>1</sup> in his investigation of the brains of general paretics and senile demented, has determined that in these cases the combined weight of the frontal and temporal lobes as compared with the weight of the parietal and occipital lobes bears a ratio of 5 to 4, while in the normal brain the ratio is 6 to 3.

In this particular case (Case I.) the mental changes were principally a change in character and disposition and apparent loss of memory.

The systemic symptoms in the same case were especially noteworthy—abnormal appetite and anorexia at different periods, great thirst, and polyuria, rise of temperature, and irregular pulse. In Cases I., II., and IV. there was vomiting. Headache was present in all four cases, being the earliest symptom in each case, except possibly Case II., when the vomiting was present at first. In all the cases except Case III. there was distinct vertigo. In all except Case IV. there was distinct optic neuritis; in this case it was only slight.

The psychic symptoms were prominent only in Case I. General convulsions were recorded in Cases I. and IV.

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## SOME PRACTICAL OBSERVATIONS ON SUPPURATIVE HEPATITIS.<sup>2</sup>

BY WILLIAM W. ASHHURST, M.D.,  
OF CHIHUAHUA, MEXICO.

AN affection so frequent in this climate deserves our deepest study and most attentive observation, more especially because unfortunately the best-known works of medicine and surgery treat this subject, for the most part, in a rather superficial and ineffectual manner, a fact which is explained by the rarity of this disease in the more advanced centres of medical science and literature.

Although it is not my present purpose to discuss the etiology, I may observe in passing that in my own experience the abuse of

<sup>1</sup> Wien med. Presse, 1886, p. 413.

<sup>2</sup> Read before the Chihuahua Medical Society.

alcohol seems to have had less influence than is generally attributed to it. I have seen a good many cases in children and women, and in men who have never used alcohol to excess. And if it is true that many cases are found in this climate in alcoholic individuals, it may also be said that a considerable proportion of the population uses alcohol excessively.

The difficulties of diagnosis are variable. Sometimes it is extremely easy, and at other times it must be made rather by exclusion than by positive symptoms of hepatic suppuration. It appears to me that when a patient suffering with acute hepatitis has not completely recovered within ten days of the commencement of the attack, aspiration is indicated, to be repeated at frequent intervals until either complete recovery ensues or pus is found. In saying *complete* recovery, I mean to imply not only apparent recovery from the hepatic affection, but that the pulse, temperature and general condition should correspond to those of health; because very often the hepatic affection seems to have disappeared, and there is found some other cause for slight febrile reaction and indisposition, such as pleural effusion, a catarrh of the intestine or a bronchitis, and it is very easy to be mistaken about the condition of the liver. These complications should be energetically treated, above all the pleural effusion. In this case it seems to me better to empty it immediately without waiting for absorption, to avoid the imminent danger of infection and suppuration of the effusion, and at the same time to facilitate observation of the liver.

It probably happens frequently, when the primary hepatitis yields and suppuration occurs in a small focus, that the general condition of the patient improves notably; the fever moderates, the pain lessens or disappears, the tongue cleans off, a little appetite returns, and the patient considers himself convalescent. But the temperature does not quite reach normal, or it may be absent only in the morning and still return at night, or conversely; the pulse continues a little frequent, and the careful observer realizes that there is still something wrong. This is probably suppuration.

This intermediate state between simple hepatitis and undoubted suppuration may last for weeks. That is to say that the hepatitis has almost disappeared by resolution, and there remains only a little spot, insignificant, causing almost no inconvenience or discomfort, but threatening from one moment to another a general conflagration; or it may be that suppuration already incipient remains for a time hidden, limited, causing no appreciable symptoms, barely allowing the physician to realize that the danger is still not over. I do not know how one can distinguish between these two conditions, apparently so much alike, unless by means of frequently repeated aspirations, which act in a curative manner toward the one and in a diagnostic way toward the other. Leukocytosis might help to solve the problem, but I have had no personal

experience with it under these circumstances, and rather doubt its practical utility. At any rate, since repeated aspiration is indicated, this will probably inform the surgeon as soon as the condition of the blood could influence the diagnosis.

Furthermore, the great difficulty is to localize the focus. Sensitiveness to deep pressure is undoubtedly the most useful sign. If there is found also localized œdema of the surface, this is a sign of great importance, but it is rare except in very large or very superficially situated abscesses.

The aspiration is best performed directly over where the focus is believed to exist; if it is done with a slender trocar (not more than two millimetres in diameter) there is no danger even if to reach the focus the border of the lung must be passed through. But often the pus is so thick that it cannot be drawn out unless a rather thick trocar is used. With this there is danger, on penetrating the lung or even the pleural cavity, of causing an infection of these organs, unless there are clear signs that the focus is very superficial, such as very marked sensitiveness, localized cellular œdema, redness of the skin or fluctuation, in which case the lung is pushed upward above its normal position, and the pleural cavity over the abscess is certainly obliterated by adhesions between the diaphragmatic and parietal pleura, and the thick trocar can penetrate to the abscess without danger. If it is necessary to pass through the lung to reach the focus, it is better to use the aspirator of Dieulafoy with a slender trocar than that of Potain, because the former gives a better vacuum, and so a greater probability of drawing out the pus through a slender trocar.

After making the diagnosis comes the delicate question of the most efficacious and least dangerous mode of emptying and draining the abscess. The simple method of introducing a tube through a thick trocar has nothing to recommend it except its simplicity. This advantage is largely neutralized by the difficulty of keeping the lumen of the tube open, since this is necessarily of small diameter. Moreover, on account of the danger of introducing a trocar large enough to accomplish its object, this method would be permissible only in very superficial abscesses with very firm adhesions between liver and diaphragm, and between diaphragm and chest wall. In these cases it is simpler and safer to make a free incision in the costal interspace, because the bistoury threatens less the integrity of the adhesions than does the thick trocar. The free incision has the advantage of allowing the introduction of one or two tubes of from 8 to 10 mm. in diameter.

H. Maasland<sup>1</sup> gives the method employed by M. Van Dyk, of Batavia. This consists in making the aspiration in the eighth or

<sup>1</sup> *Revue de gynécologie*, 6, vii, "Du traitement chirurgical des collections purulents dans le lobe droit du foie."

ninth interspace between the anterior and posterior axillary lines, the point of election. If pus is found at a depth not greater than seven centimetres he proceeds to do the operation. He does not say what he does if the focus is deeper. The presumption is that he waits for the abscess to approach nearer the surface. In case he decides to operate the patient is made to lie on his back to observe the direction which the trocar takes. Then he is turned on his left side, and with local anæsthesia (if the patient insists on general anæsthesia he uses ether) the surgeon resects six or seven centimetres of the ninth rib. Now the patient is turned again on his back, with his right side projecting over the edge of the bed or table. In this position (supine), according to Maasland, on account of the intra-abdominal pressure, there is no danger that on opening the pleura the air will penetrate. He makes the incision through the two layers of pleura, separating by dissection the diaphragmatic pleura from the diaphragm, separating the muscular fibres of the latter by means of a Kocher sound, and then incises the diaphragmatic peritoneum. He packs the borders of the peritoneal incision with iodoform gauze, and makes another exploratory puncture in the direction of the former one. Finding the abscess, he opens it with a Paquelin cautery, making in the liver a conical canal with its base outward and its apex in the focus. The longer this canal is the wider it must be. This is the reason he will not operate if the abscess is deeply seated. The destruction of healthy liver tissue would be so great that the remedy would be worse than the disease. He introduces a drainage tube of the thickness of the finger, and applies the dressing without allowing the patient to turn from the supine position until the dressing is applied, to avoid retraction of the liver and the entrance of air into the pleural cavity.

The objections to this method are to my mind various and serious. The position does not altogether remove the danger of a pneumothorax occurring. The adhesions between the layers of pleura should be fortified in a more positive manner. The destruction of liver tissue is enormous and nowise justified, and the field of operation is too limited.

Bryant in his *Operative Surgery* (1901) recommends the resection of the rib over the most prominent part of the abscess, and to avoid the entrance of air into the pleural cavity when this is opened, he makes the incision through the pleura in such a manner that two flaps are formed, one of the parietal and the other of the diaphragmatic pleura, uniting these flaps by suture before opening the abscess.

All the methods that I have seen described seem to me to have this defect: that they are adapted to the cure of only large abscesses and those situated in the most accessible regions. What is most important is to be able to cure abscesses before they reach a great size. If one waits for them to grow large and to approach the



surface one will lose many cases by perforation of the pleura and lung or by exhaustion and generalized sepsis.

The great majority of the cases seen are abscesses of the convexity of the right lobe, often situated very far from the ribs. If the abscess is situated near the edge of the liver, for example about the ninth interspace between the anterior and posterior axillary lines, or about the eighth interspace in the nipple line, a free incision may be made between the ribs without fear that the contents of the abscess will contaminate the pleura or peritoneum, because when it is so situated the slight adhesions which always exist near the abscess are sufficient to prevent the retraction of the liver or of the lung. It is different when the situation of the abscess is higher, farther upward on the convexity of the liver. Here there is imminent danger of the liver retracting, drawing with it the adherent diaphragm, tearing apart the adhesions of the recently obliterated angle of the pleura, thus permitting the entrance of pus into the pleural cavity, causing pneumopyothorax, a very serious though not necessarily fatal accident.

In the former case, where the abscess is situated near the border of the liver, I do not think the resection of a rib necessary. A simple deep incision in the costal interspace is sufficient. In the second case it is always proper to resect one or more ribs in order to reach the abscess, and to reinforce with sutures the adhesions of the pleural angle in order to allow the chest wall to retract in coincidence with the hepatic retraction. The rib which should first be resected depends somewhat on circumstances. A rib should be selected beneath which the parietal and diaphragmatic pleura are certainly in contact. To be sure of this it is well to commence far enough down, and if necessary one can work upward later. The resection of the rib, generally the ninth or the eighth, is done in the vertical line of the abscess. The resection should be done subperiosteally and taking care not to open the pleura. Having removed the bone, two silk sutures are introduced in a transverse direction, through the periosteum near its upper border, taking care that the needle reaches the diaphragm, so that the sutures unite this to the thoracic wall. It is easy to tell by the sense of touch when the needle catches the diaphragm. These two sutures are usually enough. It is unnecessary to place others below, but if a third seems to be required it can be put on the same line as the first two. These sutures should have their ends left long to facilitate their removal. I much prefer silk sutures for this purpose, but no doubt catgut would answer the purpose. After tying the sutures an incision is made parallel with the ribs and the sutures, through the middle of the inner layer of periosteum, and immediately below the sutures. This incision will penetrate the diaphragm and liver and will reach the abscess unless this is situated higher on the hepatic convexity. In this case the incision is made only through

the diaphragm, and the abscess is sought for by passing the finger between the diaphragm and the liver. The site will be recognized by the adhesions which will be found between liver and diaphragm. Where these are firmest will be found the abscess. These adhesions are, I believe, always of sufficient density to prevent any peritoneal complications; abscesses so near the edge of the liver as to endanger the peritoneum may be isolated by gauze packs, but are best treated by the abdominal route. If the abscess is so far up on the convexity of the liver that the finger cannot reach it, another rib or two must be resected above, or as many as may be necessary. This will give ample room for the finger to reach the abscess without making another diaphragmatic incision. With the finger or knife the abscess is opened and drainage tubes introduced. It is my custom not to wash out the cavity for four or five days after the operation, to give time for firm adhesions to form between the liver and diaphragm, and then for irrigating I use a solution of permanganate of potassium of 1 : 2000.

In conclusion it may be said that this method may be readily modified according to the circumstances of the case and the judgment of the operator. For example, if the abscess is large and very high, it will be better to choose for the first resection the highest rib of those over which there is absolute dulness on percussion, if in the interspace above there is intense sensitiveness.

When very firm adhesions are found between liver and diaphragm it seems to me better not to separate them, but to search for the abscess by making with the finger a dissection of the capsule of the liver from the liver substance. In this case the pus will be very near the surface of the liver, and probably the finger itself will soon open the cavity. When it is necessary to resect ribs, it seems to me better to use general anæsthesia with ether or chloroform.

## REVIEWS.

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A PRACTICAL TREATISE ON MEDICAL DIAGNOSIS. FOR STUDENTS AND PHYSICIANS. By JOHN H. MUSSER, M.D., Professor of Clinical Medicine in the University of Pennsylvania, etc. Fifth edition, revised and enlarged. Illustrated with 395 wood-cuts and 63 colored plates. Philadelphia and New York: Lea Brothers & Co., 1904.

THAT a fifth edition of Dr. Musser's work on *Diagnosis* should be so soon called for is not only flattering to the book, but is as well a most encouraging sign of the state of mind of the medical public in this country. No better proof could be furnished of the steady rise in medical standards than such evidence of a widespread recognition of the need for aid to accurate and scientific diagnosis.

In this edition there has been not only a revision but a very considerable rearrangement and rewriting of the subject-matter, and in spite of condensation in certain theoretical portions the volume has grown to the extent of some one hundred pages. The book is most lavishly supplied with illustrations, among which are many really beautiful colored plates. These cuts and plates have been selected with judgment, and have, for the most part, the not too common merit of actually illustrating the text.

The book is divided into the two distinct parts of General and Special Diagnosis, the former occupying somewhat more than half of the twelve hundred pages.

Under General Diagnosis are taken up in succession the subjects of Historical, Subjective, Objective, Physical, and Laboratory Diagnosis. This portion of the work is truly admirable. There is presented here a vast amount of information of the highest value for diagnostic purposes, and the matter is well arranged, the descriptions are clear, and the illustrations effective.

Of the second part of the book—Special Diagnosis—we can speak with quite the same enthusiasm. The separate diseases are here taken up in order, and their etiology, symptoms, complications, and diagnosis described in a manner differing from that of the usual text-books on medicine in its comprehensiveness.

We should have been glad to see the general description of many of the diseases presented in more condensed form, and greater space given to a discussion of the points of differential diagnosis.

The section on Nervous Diseases is the only chapter of Special Diagnosis which is in the least degree disappointing. It has not been given its proportionate share of space, and in it differential diagnosis is not considered at all. The brief descriptions of the clinical features of each disease are satisfactory as far as they go, but even in such important diseases as tabes dorsalis, multiple neuritis, cerebral hemorrhage, epilepsy, etc., one seeks in vain for a mention of other affections which might be confused with the disease in point.

Although the book may not perhaps maintain, in all its subdivisions, the same high plane of excellence, it nevertheless, as a whole, merits its great popularity and its position as the standard work on medical diagnosis in English, and both Dr. Musser and the profession at large are to be congratulated upon the appearance of this new edition.

L. A. C.

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A TEXT-BOOK OF MECHANOTHERAPY PREPARED FOR THE USE OF MEDICAL STUDENTS, TRAINED NURSES, AND MEDICAL GYMNASTS. By AXEL V. GRAFSTROM, B.Sc., M.D., late lieutenant in the Royal Swedish army; late House Physician, City Hospital, New York; Attending Physician to the Gustavus Adolphus Orphanage, Jamestown, N. Y. Second edition, revised and enlarged. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THE second edition of this book contains some additions and revisions. Two new chapters are added—on the massage of eye, ear, nose, and throat, and on pelvic massage.

The presentation of this subject by a man of recognized medical position undoubtedly does much toward lifting a really useful system out of the quagmire of quackery into which it has to a great extent fallen in this country. The name, mechanotherapy itself, is, to say the least, a poor title, and adds to the general air of mysticism so necessary to the successful quack.

The author describes at length general and special massage and medical gymnastics, aiding the text with illustrations of the most important postures and movements.

Then follows several chapters on the application of the treatment to special diseases. While undoubtedly general massage and medical gymnastics are beneficial in both health and disease, yet the optimism of the writer has led him to make certain statements that are scarcely capable of proof. To quote an instance: in speaking of massage and gymnastics in labor the author gives an example of a woman who in a former labor had difficulties owing to the large size of the child and the loss of flesh and strength in the mother. He then goes on to say that with the knowledge of the former diffi-

culties mechanotherapy may be so applied during a subsequent pregnancy that the "development of the fœtus will be retarded, and after a normal and comparatively easy labor a normal-sized child will be born." While this result might be the aim of the treatment, the proof of the effect is most difficult. Without being guilty of too great a *reductio ad absurdum*, we might demand of a mechanotherapist the exercise of his skill in the production of blue or more probably of black eyes in the coming baby.

In regard to uterine massage, with many others, we feel that the less said or done the better. On the whole the book should prove useful to those for whom it was written, students, nurses, and medical gymnasts.

J. N. H.

PRACTICAL MATERIA MEDICA FOR NURSES, WITH AN APPENDIX CONTAINING POISONS AND THEIR ANTIDOTES, WITH POISON EMERGENCIES, MINERAL WATERS, WEIGHTS AND MEASURES, DOSE LIST, AND A GLOSSARY OF THE TERMS USED IN MATERIA MEDICA AND THERAPEUTICS. By EMILY A. M. STONEY. Second edition, thoroughly revised. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THIS volume is written with the idea of being an adjunct to *Practical Points in Nursing*, by the same author.

The description of the drugs is confined to their source, their action and uses, dosage and symptoms, and treatment of poisoning, and the drugs themselves are arranged in alphabetical order. A final chapter on Poison Emergencies, Mineral Waters, Weights and Measures, Dose List, and Glossary bring the book to a conclusion. As a book of reference for nurses it should meet the demand, as it has the virtue of omitting the unnecessary.

J. N. H.

A REFERENCE HANDBOOK OF THE MEDICAL SCIENCES EMBRACING THE ENTIRE RANGE OF SCIENTIFIC AND PRACTICAL MEDICINE AND ALLIED SCIENCE. By various writers. A new edition, completely revised and rewritten. Edited by ALBERT H. BUCK, M.D., New York City. Volume VIII. Illustrated by chromolithographs and 435 half-tone and wood engravings. New York: William Wood & Co.

THIS last volume of the new edition of the *Reference Handbook* brings this encyclopedic work to a worthy close. The articles which it contains are of the same high standard that has characterized those in previous volumes, and the same amount of editorial

care is manifest throughout. In an appendix there is introduced a large amount of valuable addenda to articles which have appeared in the previous volumes. There is also a most excellent index to the entire set. We know of no one work in American medicine which is more worthy of a place in every physician's library than this; it constitutes a complete encyclopedia of medicine and the allied sciences, and the information which it contains may be confidently relied on as thoroughly accurate. F. R. P.

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FRIEDBERGER AND FROHNER'S VETERINARY PATHOLOGY. (Authorized translation.) Translated and edited by W. H. HAYES, F.R.C.V.S., with notes on Bacteriology by DR. C. NEWMAN, D.P.H. Volume I. London: Hurst & Blackett, Ltd. Chicago: W. T. Keener & Co., 1904.

NOT only is the *Lehrbuch der speciellen Pathologie und Therapie der Hausthiere*, of which this book is a translation, one of the highest authorities on veterinary medicine in Germany, but the French translation has been widely adopted in France. This authorized English translation cannot fail to be of great value to the veterinarian, and should, moreover, attract the interest of the physician. The first volume deals particularly with the infectious diseases of domestic animals, a subject which is rapidly becoming of practical importance to the clinician, and has always been of great interest to scientific medicine.

Practically all of the contagious and infectious diseases of the domestic animals are considered at some length, and to the more important, such as anthrax, tuberculosis, etc., several pages are devoted. Each disease is considered in all its phases, and the paragraphing is excellently arranged. In the second chapter one finds descriptions of the miscellaneous infectious diseases, while the third chapter takes up the chronic constitutional diseases. The fourth chapter forms an addenda to the infectious diseases inserted by the translator. Here surra, tsetse-fly disease, South African horse-sickness, diseases conveyed by ticks and other conditions are discussed, but owing to the unsettled state of our knowledge of some of these affections and the rapid progress which is daily being made concerning their etiology and classification, this chapter will doubtless need revision. The notes on bacteriology, written by Dr. Newman, fall very short of the rest of the volume, both in completeness and in scientific exactness.

In fact, the value of the book rests essentially upon the broad and scientific treatment of the subject. The binding is poor, unattractive, and does not prepare one for the excellence of the text, which

however, is well printed. Where it was thought necessary to bring a subject up to date, the translator has added notes throughout the volume.

W. T. L.

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ORGANIC AND PHYSIOLOGIC CHEMISTRY. THE MEDICAL EPITOME SERIES. By ALEXIUS MCGLANNAN, M.D., Associate Professor of Physiologic Chemistry, College of Physicians and Surgeons, Baltimore, Md. Philadelphia and New York: Lea Brothers & Co., 1903.

THIS small manual in less than 250 pages covers in a very complete manner the essentials of organic and physiologic chemistry. Numerous diagrammatic formulæ of structure and reaction occur throughout the book and aid graphically in the explanations and the discussion of the various vital processes and of metabolism is presented in a thoroughly comprehensible manner.

A table of food composition and fuel values of a number of common food articles is submitted in the appendix. The book furnishes a very accurate summary of the latest knowledge in a rapidly advancing science compiled in such a manner as to render it especially adapted for use by the student.

F. F.

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PATHOLOGICAL TECHNIQUE. A Practical Manual for Workers in Pathological Histology and Bacteriology, including Directions for the Performance of Autopsies and for Clinical Diagnosis. By FRANK BURR MALLORY, A.M., M.D., Associate Professor of Pathology, Harvard Medical School; First Assistant Visiting Pathologist to Boston City Hospital; Pathologist to the Children's Hospital, and JAMES HOMER WRIGHT, A.M., M.D.; Director of the Clinico-Pathological Laboratory of the Massachusetts General Hospital; Instructor in Pathology, Harvard University Medical School. Third edition, revised and enlarged, with 156 illustrations. Philadelphia: W. B. Saunders & Co., 1904.

THE third edition of this book, like the former editions, is of undisputed value, while the work remains as always an authority on laboratory technique. The general convenient arrangement of the subject-matter which is so well known suffers no essential change. New material has been added, principally to Parts II. and III. Among the most notable additions in Part II. are: Hill's hanging-drop method; Harris' celloidin sac method; methods for isolation of typhoid bacilli from feces, and sections on the bacilli of dysentery and of chancroid, containing certain improvements in the

methods of their isolation. Many very important additions have been made to Part III. Among these are: Improved methods for embedding and manipulating frozen sections, by Wright, most useful contributions which have not been published before; the latest staining methods of Weigert, Wright's blood stain, already familiar to many; the technique of cytodagnosis and inoscopy, methods which have recently become of much practical value in the examination of serous fluids; Mallory's stain for fibroglia fibrils, besides many other staining methods which have recently been devised. The book is so well known and has been so widely used that to praise it would be superfluous. In the laboratory it has become a necessity.

W. T. L.

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A SHORT TREATISE ON ANTITYPHOID INOCULATION, CONTAINING AN EXPOSITION OF THE PRINCIPLES OF THE METHOD AND A SUMMARY OF THE RESULTS ACHIEVED BY ITS APPLICATION. By A. E. WRIGHT, M.D., University of Dublin, late Professor of Pathology, Army Medical School, Netley; Pathologist to St. Mary's Hospital, Paddington, W. Westminster: W. Archibald Constable & Co., 1904. W. T. Keener & Co., American agents.

For the last few years Dr. Wright's name has been so closely associated with the subject of antityphoid inoculation, and his experimental work has led to such interesting and important results in this field, that a *résumé* of the methods and outcome of his investigations embodied in this small book cannot fail to be of value. The book is based on three papers dealing with antityphoid inoculation contributed to the *Practitioner*, and reprinted here with amplifications. The preliminary chapters give a brief exposition of the scientific principles involved in antityphoid inoculation, in which it is shown that inoculation of cultures of typhoid bacilli which have been sterilized by exposure to a temperature of 60° induces in the organism an elaboration of certain protective substances. These the author designates as agglutinating antitropines, bacterial antitropines, bacteriolytic antitropines, antitoxic antitropines, and opsonic antitropines. The author's method does not consist in the use of an antityphoid serum, but in actual vaccination by the inoculation into the individual of sterilized cultures of typhoid bacilli. The injections are followed by a definite local and constitutional reaction. At the site of inoculation there is pain and slight swelling, while for several hours, and when large doses of the vaccine are used, for a few days afterward, the individual may suffer from general malaise, headache, and slight fever. The inoculations have never been attended with serious accident. Finally, in the fourth chapter there follows the statistical records compiled from about 100,000



inoculations of British soldiers in South Africa and India. These records are reviewed in a perfectly impartial and indeed critical manner. As they stand they show a mortality from typhoid fever of 8 per cent. among 1758 inoculated patients, and a mortality of 16.6 per cent. among 10,980 uninoculated persons. An appendix furnishes a detailed description of the procedures employed for preparing and standardizing antityphoid vaccine, while a second appendix gives a list of the author's papers dealing with immunization and kindred subjects. The book is interesting, well printed, and well bound.

W. T. L.

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STRABISMUS; OR SQUINT, LATENT AND FIXED. A SUPPLEMENT TO THE ERRORS OF REFRACTION. By FRANCIS VALK, M.D., Professor of Diseases of the Eye, New York Post-Graduate School and Hospital; Consulting Ophthalmologist, Thrall Hospital, etc. New York and London: G. P. Putnam's Sons, The Knickerbocker Press, 1904.

THIS is a very difficult book to read. The style is diffuse, obscure, and rambling; so much so that only the reader well acquainted with the subject-matter with which the work deals can, in a measure, comprehend what the author means by supplementing its deficiencies from his own knowledge, and even there are passages the meaning of which will baffle him to decipher.

The writer insists that there is a single underlying cause of heterophoria and heterotropia. He rejects the classical explanation of the dependence of the deviation upon the refraction given by Donders, as well as the views of many other writers upon the subject, such as the innervation hypothesis, and strongly urges that "the essential cause of all squint is a weakness of some one or more muscles of the eyeball." He argues that the recti alone are concerned in moving the eyes in different directions in the field of fixation, and limits the function of the obliques to maintaining the parallelism of the vertical planes of the eyes.

In the diagnosis of heterophoria the author lays stress upon the relative power of fusion of the different muscles as measured by prisms. If this agrees with the standard, for example, the adducting power being three times that of the abducting, the eyes will be free from muscular deficiency. He regards this test as of greater value than those in which binocular vision is first abolished, such as the diplopia test and the Maddox rod, arguing that the former conforms to a normal condition, while the latter substitutes an artificial one.

As regards the treatment of the various forms of heterophoria, while recommending that a trial be first made of the usual and less

radical measures, correction of any existing ametropia, prism exercises, general hygiene, etc., the writer is strongly disposed toward operative procedures, particularly that of shortening a weak muscle by a "tuck" with catgut suture, for which operation he claims excellent results.

The author makes an interesting distinction in the amblyopias of squint—congenital amblyopia and *amblyopia exanopsia*. In the former—vision less than  $\frac{20}{100}$ —improvement will be found impossible; operative measures are useful only from a cosmetic point of view. The latter, *amblyopia exanopsia*, are capable of great improvement, and even of restoration of binocular vision.

Upon the whole, this book strikes us as an honest expression of a conscientious worker's individual views based upon personal experience. The author throws out a number of interesting and suggestive hints. We hope for the sake of its merits that the writer will devote more care to the style in subsequent editions.

T. B. S.

A TEXT-BOOK OF DISEASES OF THE NOSE AND THROAT. By D. BRADEN KYLE, M.D. Third edition, revised and enlarged. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THE present edition of this excellent text-book contains some noteworthy new material. It is rare to find a text-book elaborating some really new views based on its author's original investigations. Dr. Kyle has worked up a new and most plausible and ingenious theory to account for that mysterious entity which is generally known under the name of hay fever. It is based on sialosemeiology or the study of the saliva. By a long course of laboratory work and clinical study he has come to the conclusion that in many cases the symptoms which are present in hay fever are the result of alterations in the character of the secretion of the mucous secreting glands. This alteration is manifest clinically in a change of the reaction of the secretion; thus when the saliva is in a condition of hyperacidity we find sulphocyanide present in excess. When the saliva is hyperacid, ammonia salts are in excess. In a number of instances in which Dr. Kyle has given substances to alter the reaction of the secretion there has been a marked alleviation of the symptoms. As the author distinctly states, it will require the study of many more cases and much laboratory investigation before this theory can be absolutely proven; nevertheless, he has done sufficient work to make it very essential that further research should be carried out along his lines.

There is a very full and fair account of the use of paraffin injections for the correction of nasal deformities,

The previous editions have met with such a deservedly cordial reception that there is no doubt that the present edition with enlargement will be received with even more favor than its predecessors.

F. R. P.

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THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Under the general editorial charge of GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Post-Graduate Medical School. Volume X. Skin and Venereal Diseases, Nervous and Mental Diseases. Edited by W. L. BAUM, M.D., and HUGH T. PATRICK, M.D. Chicago: The Year Book Publishers.

THIS volume gives to the reader a good idea of the general progress of medicine during the current year in the fields of dermatology and venereal and nervous diseases. It consists of a carefully selected *résumé* of the latest literature on these subjects.

Included in the section on skin diseases is a short but interesting chapter on Actinotherapy and Radiotherapy. The chapter on Syphilis is devoted to a great extent to the consideration of the experimental attempts on the transmission of this disease to the lower animals.

There is a good deal in the section on Nervous Diseases that will be of some value to the general practitioner, especially that part devoted to the Symptomatology.

The material is necessarily much condensed, but there has been no sacrifice of clearness to brevity. The volume contains a number of illustrations.

A. N.

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THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. GYNECOLOGY. By E. C. DUDLEY, A.M., M.D., and WILLIAM HEALY, A.B., M.D. Chicago: The Year Book Publishers, 1904.

WE feel sure that the profession at large will give a most favorable verdict after reading this little book. To those who are acquainted with the volumes of former years it is unnecessary to say more than that the present book is fully up to the average of its predecessors. The illustrations of the original articles are introduced in several of the abstracts and greatly enhance the value of the work.

W. R. N.

# PROGRESS OF MEDICAL SCIENCE.

## MEDICINE.

UNDER THE CHARGE OF

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Some Observations on the Etiology, Morbid Anatomy, and Associated Pathology of Bronchiectasis.—D. BARTY KING (*Scottish Medical and Surgical Journal*, June, 1904, p. 481) reports that 72 cases of bronchiectasis occurred at the Brompton Hospital for Diseases of the Chest out of a total of 3227 autopsies on patients dying of pulmonary diseases. This made 2.2 per cent. of the total autopsies, and corresponded closely with the statistics of Biermer, who records 2 per cent. Willigk found 8 per cent. out of 4517 autopsies.

Cases not associated with tuberculosis are spoken of as "pure bronchiectasis;" those associated with tuberculosis as "tubercular bronchiectasis," and those resulting from effects of aortic aneurism, mediastinal tumor, foreign bodies and syphilitic strictures, as "traumatic bronchiectasis." The disease originates in early and middle adult life. Data as to age were obtainable in 64 cases. Of these, 53.1 per cent. died between the ages of twenty and forty years. A fatal termination usually occurs earlier in the tubercular than in the pure bronchiectasis cases. King was able to determine the type of the affection in seventy instances. There were 36 pure, 9 traumatic, and 25 tubercular cases. The disease predominates in males, 77 per cent. being males and 23 per cent. females in his series. There were no females among the traumatic cases. There was a tuberculous family history in 41 per cent. of the tubercular and in 14 per cent. of the pure and traumatic cases. The mode of onset was determined in 64 cases. In 75 per cent. it followed a chronic bronchitis; in 11 per cent. a lobar pneumonia; in 11 per cent. a pleurisy, and in 3 per cent. a pleuropneumonia.

Whooping-cough and influenza were the most frequently associated diseases, and the author emphasizes the importance of the latter as an etiological factor.

In 69 of the cases analyzed the bronchiectasis was bilateral in 62.3 per cent., and unilateral in 37.7 per cent. In the unilateral cases the right lung was more often affected than the left.

Of associated pathological lesions pericardial adhesions were the most frequent. They occurred in 18 per cent. of the cases. Pericarditis with effusion occurred in 5 per cent. of 70 cases, all in the pure bronchiectasis type. Cerebral abscess was present in 8 of the 72 cases, or in 11.1 per cent. Hypertrophic pulmonary osteoarthropathy occurred in several instances, the exact number not being stated.

**Perforating Ulcer in General Paresis.**—E. MARANDON DE MONTYEL (*Revue de médecine*, June 10, 1904, p. 497) reports the clinical records of 15 cases of perforating ulcer occurring in patients suffering from general paresis. He had recorded 5 other cases in 1882, and at that time expressed the opinion that the complication occurred more frequently than is generally supposed. His interne, M. Barthelemy, had published 4 additional cases in his doctor's thesis, so that the writer has altogether observed 24 cases of general paresis with perforating ulcer. The 15 cases of perforating ulcer here recorded were out of a total of 500 cases of general paresis. The complication, therefore, occurred in 3 per cent. of the cases. In 14 of the cases the perforating ulcer occurred on the feet, and in 1 case the upper lip was involved.

The complication may occur during any stage of the disease. An important fact brought out is that it may antedate the onset of the general paresis symptoms. Montyel considers that alcohol is an important etiological factor. Of the 24 cases he has observed, a history of its excessive use was obtained in 22. Perforating ulcer is more likely to occur early than late in the disease, and the writer thinks that the tendency of the paretic in the early stages to be constantly on his feet and to walk about more than usual is responsible for this fact. He has noted that the development of an ulcer may cause an amelioration in the patient's general symptoms. On the other hand, a cure of the ulcer has been observed to aggravate them and apparently to even hasten death.

**Multiple Sclerosis: Its Occurrence and Etiology.**—JELLIFFE (*Journal of Nervous and Mental Disease*, July, 1904, p. 446) has analyzed the cases of multiple sclerosis admitted to the Vanderbilt clinic under Dr. M. Allen Starr since its opening in May, 1888, up to January 1, 1904. There were in all 109 cases, or 0.0034 per cent. of the total neurological cases, or about 1 in 300. By comparison with English and German statistics he shows that the disease is more common in those countries than in the United States.

There were 68 males and 41 females. The statistics of other observers also show males to be a little more frequently affected than females. The largest number of cases—27—occurred between the ages of thirty and forty years. The youngest patient was four years old, and there were 9 patients under ten years of age. The oldest patient was sixty-eight years old. The character of the patients' occupations apparently bore no relation to the development of the disease. Hereditary influences did not appear to play an important part. Although the writer's cases do not forcibly support this point, yet he is inclined to agree with Le Brun and Hoffman that the disease is in many cases due in part to a previous infectious disease. Among the infections, however, syphilis does not appear to be a potent factor. There was a history of trauma in 13 of Jelliffe's cases. It was present in 10 per cent. of Hoffman's

cases. It cannot be said that the organic and inorganic poisons are very important as etiological factors. According to Oppenheim, lead may be the cause in some cases. The influence of alcohol is believed to be of minor importance.

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**Isolated Tuberculous Pericarditis.**—G. SCAGLIOSI (*Deutsche med. Woch.*, 1904, xxx., 873) reports the case of a woman, aged sixty years, who died of pyelonephritis. At the autopsy, as an accidental finding, there was a well-marked tuberculous pericarditis, *the only tuberculous lesion that could be found in the body*. All of the organs were carefully examined, the pulmonary apices and the bronchial, tracheal, and cervical lymph glands especially. Neither macroscopically nor microscopically could any tubercles be found. Scagliosi was able to collect only seven similar cases from the literature. Involvement is common in miliary tuberculosis; it is rarely transferred directly from the lungs or pleura. The most frequent source of infection—indeed, the source in nearly all cases—is tuberculous mediastinal glands.

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**Pseudoascites as the Result of Chronic Enteritis.**—L. TOBLER (*Deut. Archiv f. klin. Med.*, 1904, lxxx., 288) reports a very interesting group of cases showing clinically the classical signs of free fluid in the peritoneal cavity, while at operation or autopsy a perfectly normal peritoneum was found with no sign of the anticipated exudate. The cases suggested very strongly tuberculous peritonitis, especially those in which there was a tuberculous lesion elsewhere. This, indeed, is the diagnosis with which most of them were transferred to the surgeons. On the basis of these observations Tobler draws a clinical picture which may serve to put one on his guard in dealing with similar cases. All of the instances occurred in children, the youngest two and one-half years, the oldest nine years, the average age six years. In all there is a history of continuous or recurring diarrhoea for months or years, followed by a gradual enlargement of the abdomen. In some the origin of the trouble could be traced to injudicious feeding, while nearly all had been neglected or improperly treated. The general condition had suffered severely, most of the patients being weak, sickly children, poorly nourished, and often extremely emaciated. Some showed definite rachitic deformities, others tuberculous bone lesions or masses of enlarged glands. There are no subjective symptoms other than occasional complaints of abdominal pain. The prominent uniformly swollen abdomen stands out in marked contrast with the emaciated chest and extremities, and on palpation feels firm, elastic, and resistant. This picture is, however, not constant, as the abdomen may be only moderately enlarged, feel soft and flabby, falling from side to side with change of posture, while the intestinal coils are visible. These differences are observed not only in separate cases, but in a single case the conditions may change with surprising rapidity. In all of these cases a definite undulation could be felt, and in many there was distinct shifting dullness. The areas of percussion dullness vary within wide limits in different cases and in the same case from day to day. They may be those commonly found in ascites or more irregular in disposition. The most important differential diagnostic points from tuberculous peritonitis are the absence of fever and of all but very mild abdominal pain, the rapid change in the condition of the patient, the

history of long-continued diarrhoea, and the frequent irregularities in the areas of dulness, the pattern changing from day to day. None of these points are, however, distinctive, and one can judge how uncertain the diagnosis may be.

The essential symptoms in these cases is the swollen abdomen, giving the definite sensation of a fluid wave. Tobler refers this condition to the fluid contents of the intestines, and from the position of the dulness concludes that the coils of the ileum are especially affected, the colon perhaps assisting to give the flank dulness, while atony of the intestinal wall and a lax mesentery allowing the coils to fall from side to side are probably important factors.

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**The Occurrence of Pentosuria as a Family Anomaly.**—M. BIAL (*Berl. med. Wochenschrift*, 1904, xli., 552) reports the very interesting and important observation of the occurrence of pentosuria in two sisters and a brother. He also had the opportunity of examining the urine of the father, two other brothers and a daughter of each of the affected sisters, in all of whom pentose was absent. The symptoms in these cases were purely neurotic. They had all been told they had sugar in their urine, and the brother particularly was much depressed by the knowledge of this family disposition to diabetes. These cases are of importance from two standpoints. They emphasize the tendency of the condition to occur in families, Blumenthal having previously reported two cases in one family, and they again direct attention to the ease with which the benign pentosuria is confused with the more serious glycosuria, pentose and glucose both readily reducing Fehling's solution. Bial has devised a very simple test to differentiate the two, the method of procedure having been previously described in the *Deutsche med. Woch.*, 1903, No. 27. The required solution consists of 30 per cent. hydrochloric acid, 500 c.c.; orcin, 1 gram; liquor ferri chloridi, 25 drops. A portion of this is heated to boiling, the test-tube then withdrawn from the flame, and a few drops of urine added. In the presence of pentose a beautiful green color is produced.

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**Hysterical Ileus.**—EDWARD SCHWARTZ (*St. Petersburger med. Woch.*, 1904, xxix., No. 21, 225) reports an interesting case of hysterical ileus in a girl, aged twenty-one years. Her mother had died six years before of volvulus, and a sister four months before of the same condition. The patient, who had nursed her sister and was present during the attacks of fecal vomiting, was taken ill with the same symptoms that characterized the onset of the sister's illness. On admission to the hospital she complained of nausea and pain in the abdomen; a distinct mass was felt in the left inguinal region. The nausea was followed by vomiting, the pain became very severe, and the abdomen was distended. Operation revealed a perfectly normal condition of the intestine. The mass, which was scybalous, was easily dislodged by manipulation. After a brief period of improvement the symptoms recurred. There was absolute constipation for twenty-two days, during which period there was frequent fecal vomiting, and no food could be retained. The fecal vomiting usually followed enemata, which were always ineffectual. For five weeks longer there was no improvement, while the patient became very emaciated. Pain in the abdomen, constipation, and attacks of fecal vomiting persisted. During the whole period exami-

nation was negative except for slight distention of the abdomen and a little tenderness. After having been in the hospital three months recovery began, and progressed rapidly, with isolation and suggestion. She was throughout exceedingly neurotic, and on several occasions was thrown into violent hysterical crises by intimations that her disease was simulated.

While such instances are unusual they are not extremely rare. Bregmann, in 1901, was able to collect from 15 to 20 cases from the literature. They occur in young men and women usually with typical hysterical stigmata, and simulate chronic peritonitis, appendicitis, and intestinal obstruction. Fecal vomiting has occurred in such cases at intervals over a period of six years. One of Sanders' patients was operated upon twice, the other four times, and Treve's patient three times. The probable explanation of these cases is the occurrence of antiperistaltic movement of the bowel. Such a possibility is amply demonstrated by experiment. Kinstei resected a piece of intestine and reunited it in the opposite direction; Mühsam practically inverted the whole small intestine, and in both experiments the normal movements from stomach to rectum were immediately begun. In Treve's case starch and bismuth were injected into the rectum and recovered in the vomitus.

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## SURGERY.

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UNDER THE CHARGE OF

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**A Note on the Treatment of Syphilis.**—JONATHAN HUTCHINSON (*Practitioner*, August, 1904) states that it is his belief that the profession is now settling down into the conviction that crude mercury is the one specific for syphilis, and that there is no more effectual way of using it than by rubbing it into the skin. Those who prefer administration by the mouth, of whom the author is one, do not do so in the belief that it is more effectual but simply because it is more convenient. The modern use of mercury against syphilis has been embarrassed by knowledge which our forefathers did not possess. For them all sores on the genitals resulting from impure intercourse were specific, and for all mercury pushed to the point of ptyalism was prescribed without compunction. Thus it is not improbable that the entire suppression of the disease in its very beginning was often accomplished. Recent experience has conclusively shown that by beginning mercury before the development of secondary symptoms that stage may be entirely



prevented, and the patient may never know more of the malady than the primary sore. The earlier the remedy is commenced the more effective it appears to be in attaining this object. It should be remembered, however, that in no case should specific treatment be begun until the diagnosis is absolutely established. Experience has shown that the anticipation of the secondary stage and the prevention of its development is of paramount importance in preventing symptoms of the tertiary class. The author states that space does not permit him to go fully into the question as to not only how early mercury should be commenced as well as how long it should be continued, and whether the treatment should be an interrupted or a continuous one. Briefly, in his own experience, excellent results have been obtained by the application of the following plan of treatment: A pill is prescribed containing one grain of gray powder and one of Dover's powder, and this the patient is to take after meals, and only three times a day at first. If no diarrhoea follows after a few days the pill is to be given four, five, or six times a day. All soups, fruit, and green vegetables are peremptorily forbidden, and from the first the patient is told that the treatment and the precautions must be continued without any intermission whatever for a year at least. An alum mouth-wash is prescribed, with a view to prevent pyalism. The patient is allowed to continue his ordinary occupation, but is advised to spend as much time in bed as he can suitably manage. If there is debility a grain of quinine is added to the pill, and under this plan of treatment it is very rare to see any symptoms either on the throat or on the skin. In the author's experience the iodide of mercury has proven much less manageable than when these two drugs are given separately, and, as a general rule, in his practice, the use of iodides is avoided in all the early stages. Their value in the treatment of tertiary gummata cannot be overestimated.

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**The Operative Treatment of Habitual Luxation of the Patella.**—KRUGINS (*Centralblatt für Chir.*, 1904, No. 9) states that he has had good success with the following method:

1. On the outer side of the patella is made a bow-shaped incision of the skin. The inner portion of the knee capsule should then be loosened, as should also the lateral skin edge, so that a free exposure of the joint can be made.

2. An incision should be made longitudinally to the outer edge of the patella at a point a finger's width from the upper half of the patella to the insertion of the ligament patella, this incision being through the true fibrous capsule as well as the synovial membrane.

3. Longitudinally to the inner edge of the patella an incision is made from the point of junction of the ligament patella to a point in the vastus muscle, following as far as possible the direction of the fibres of this muscle, and then a second incision about two fingers' breadth to the inner side should be made; by the dissection of these tissues from the synovial membrane a bridge-shaped rim of tissue is formed.

4. The longitudinal loss of tissue which results from the further dissection of these incisions should be closed with strong catgut sutures.

5. Then the bridge-shaped rim should be carried to the outer edge of the patella and passed into the space which is the result of the fracture, and the edges should then be closely approximated with catgut.

6. The operation is completed by closing the skin incisions after making provisions for drainage. The leg should be carefully splinted for from three to four weeks, after which massage is indicated.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**Opoththerapy in Cirrhosis of the Liver.**—DR. M. HIRTZ reports an instance of this disease which, on first observation, was suffering from abundant oedema and ascites; the liver was small, the spleen much enlarged, and the collateral circulation very marked. The patient was put upon milk diet and given about four ounces of fresh pork liver mixed with bouillon. Abdominal puncture resulted in the withdrawal of four quarts of fluid besides what oozed from the wound during several days following. The urine was rapidly increased to over 90 ounces a day; this is considered a valuable prognostic sign. Gradually the oedema and the collateral circulation disappeared, and there was no return of the ascites. Unfortunately, the results in all cases are not so favorable as in this, nor are we able to distinguish beforehand the patients who are likely to improve under this treatment.—*La presse médicale*, 1904, No. 52, p. 413.

**Dechloruration in the Treatment of Pleuritic Effusion.**—DRS. CHAUFFARD and BODIN, as a result of experiments in cases of pleurisy with effusion, have found that the chlorides administered during the period of resorption of the fluid are eliminated by the urine, while during the height of the effusion their administration causes it to increase in quantity, produces a nervous agitation, due, perhaps, to slight cerebral oedema, and in large doses a condition of venous stasis, which in one patient resulted in a thrombosis of the veins of the leg, persisting three weeks, may result. Consequently, they experimented with a mixed diet lacking in chlorides and with strict milk diet. The former was not well borne, but the latter, since it produces free diuresis and promotes the chloric crisis accompanying the natural cure of the disease, was found to result most favorably.—*Gazette des hôpitaux*, 1904, No. 51, p. 497.

**Dechloruration in Dermatitis.**—M. P. RAVAUT, on account of the excellent results attained in the oedema of nephritis by means of dechloruration, has applied the method in certain dermatoses characterized

by an interstitial exudation or by the formation of crusts. In a case of the artificial dermatitis in a laundress, which showed itself as eczematous lesions on forearms and thighs, accompanied by a serous infiltration of the cellular subcutaneous tissues the treatment was tried. The patient presented no symptom of renal insufficiency, and her eruption had resisted various forms of treatment. She was put upon a diet lacking chlorides. For two days no change except a lessening in the urinary chlorides was noticed. On the third day the itching diminished, and on the fifth disappeared, together with the oedema, although the skin remained red and thickened; gradually, however, these symptoms also disappeared. As a control experiment the patient was given ordinary diet, and the dermatitis reappeared in five days, disappearing again upon a resumption of the diet without chlorides.—*Gazette des hôpitaux*, 1904, No. 48, p. 469.

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**Intramuscular Injections of Antipyrin in Sciatica.**—DR. SCHEUER has employed with success an injection of a solution of antipyrin in an equal quantity of distilled water. This is boiled for a moment and filtered through cotton. About 10 to 15 minims are injected into the region of the nerve trunk at each sitting, and the treatment must be continued at intervals of several days for a considerable time. The injection must be given deep into the muscular tissues, for simple subcutaneous injections may be followed by very painful and persistent reaction.—*Journal de médecine de Paris*, 1904, No. 24, p. 240.

DOTT. SIGISMONDO PASCOLETTE injects a 50 per cent. aqueous solution of this substance into the muscles along the course of the nerve, but especially at the site of the maximum pain. The amount employed is not stated. Rapidity of amelioration and speedy cures are claimed.—*Gazzetta degli Ospedali e delle Cliniche*, 1904, No. 70, p. 745.

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**Carbogaseous Baths in Arterial Hypotension and Hypertension.**—M. DE LAUSSEDAT, after numerous observations of patients with increased and decreased arterial tension and of the various methods of employing gaseous baths in these conditions, concludes that if the arteries are not sclerosed to the point of having lost their elasticity, if the heart muscle is sufficiently resistant, if the arterioles of the kidneys maintain a state of relative patency, and, lastly, if the vasomotor system reacts easily, it is always possible to bring about certain effects by the baths if established therapeutic indications are carried out. In hypertension the baths at first should be very gaseous and very short; the hypertension will be more influenced as the baths are gradually lengthened. The temperature is not of great consequence. In hypotension the baths should always be of skin temperature, without gas at the beginning, but progressively made more gaseous. The baths here should be of long duration. The action of the baths is always antitoxic and eliminant, since under their influence the excretion of urine is notably increased.—*Bulletin de l'Académie de médecine*, 1904, No. 25, p. 532.

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**Hydrotherapy in Tuberculosis.**—DR. KUTHI reports upon the results obtained from the hydrotherapeutic treatment of 1000 tuberculous patients. As a general rule, for those with a febrile movement

cold wet packs for four hours were prescribed; following this procedure the pyrexia was relieved, the appetite increased, and sleep was induced. Each morning the skin of the whole body was rubbed with a moist towel. These frictions improved the peripheral circulation and lessened the tendency to perspiration. The shower bath was found to be badly borne by nervous patients, and it is contraindicated in persistent fever, hæmoptysis, and pleural pain. Tuberculous patients derive great benefit from cold applications by means of Leiter's tubes or the ice-bag to the precordium. By this means tachycardia and dyspnœa are lessened. Gastric disturbances early in the disease may be combated by the application of heat, by means of Leiter's coil, to the epigastrium. In cases of gastric atony the use of cold is to be preferred; intestinal atony may be relieved by cold sitz-baths, lasting from three to eight minutes.—*Blätter für klinische Hydrotherapie*, 1904, No. 5, p. 93.

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**Hydrotherapeusis in Neurasthenia.**—M. BENI-BARDE recommends that the treatment be begun with a spray-bath at from 92° to 99°. The spray should be applied for some time along the spinal axis from above downward, but care must be exercised to guard against sudden shock, and one should endeavor to dispose the patient toward sleep. The douche should last from four to eight minutes; if it lasts longer the patient is likely to become excited rather than soothed. The back is first sprayed, then the anterior surface, and finally the limbs. Two baths a day should be given until the nervous agitation has ceased; this may take a considerable period. To stimulate the organism, the temperature of the water may be varied gradually during the progress of the procedure; any tendency toward untoward reaction may be relieved with hot water. If there is marked mental weakness the head should not be sprayed, and if the heart is affected only the lightest application of the stream over the chest is allowable. In patients with genito-urinary complications a hypogastric or perineal douche or sitz-bath in running water may be employed. Cold water is to be reserved until all excitement has disappeared. The various neuralgias from which neurasthenies suffer may be relieved by vapor baths.—*Journal des praticiens*, 1904, No. 21, p. 323.

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**Maretin as an Antipyretic.**—J. BARJANSKY reports that this drug is a non-poisonous antifebrin. Chemically it is a methylated acetanilid. It is a white, shiny, tasteless, crystalline powder, difficultly soluble in water. Animal experimentation shows it to have no influence upon circulation or respiration. It is antipyretic in doses of 1½ grains, and doses of 15 grains cause no toxic symptoms. In human beings it does not affect either the respiration, digestion, urinary system, or the condition of the blood. Its excretion by the urine begins in a half hour after its administration, and its antipyretic effect in three-quarters of an hour. At first the temperature falls slowly, but later more rapidly, the effect lasting from fifteen to twenty-four hours. The drug is indicated in the fever of phthisis, typhoid fever, malaria, sepsis, influenza, etc. In phthisis the beginning dose of 3 grains may be increased later to 7. From observations of 10 phthisis patients, it appears that marctin is an antipyretic of certain and lasting effect. It is best given in powders of 3½ grains, morning and evening, washed down by a swallow of water.

The only bad effects noticed were in 1 patient, who suffered from transitory symptoms of collapse. There is no cumulative effect. The fall in temperature in the phthisis patients was often accompanied by sweating, consequently an examination into the effect of agaricin simultaneously given with the maretin is suggested by the writer.—*Berliner klinische Wochenschrift*, 1904, No. 23, p. 607.

- **Massive Mercurialization in Tabes.**—M. VAUDY considers that injections of the soluble salts are preferable to inunctions or to injections of the insoluble salts. He advocates a solution of the benzoate of mercury, which is less toxic and better borne than the biniodide. Of this he gives intramuscular injections, commencing with  $\frac{3}{16}$  grain, increasing the dose daily by half that quantity until symptoms of poisoning appear. Having ascertained the quantity which can be borne, the patient is given this dose indefinitely. Of 4 cases treated, 1 received 500 injections in less than three years, the other 3 about 300. Three of these were admittedly syphilitic, the fourth denied infection. All were in the stage of inco-ordination; their symptoms became ameliorated, and some of them disappeared altogether. The treatment, necessitates great patience on the part of both physician and patient and should be continued for several years.—*Le Marseille médical*, 1904, No. 7, p. 193.

**Collargol in Diphtheria.**—MM. GUINON and NETTER base their report upon collargol in diphtheria upon a large number of cases treated during 1903 with both inunctions and intravenous injections of the substance. Every patient when first seen received an inunction, and in the severe cases were given intravenous infusions as well. The treatment was followed in most cases, both of toxic and hypertoxic diphtheria, by recovery. Statistics given by the authors show a noticeable decrease in the mortality over years in which the same treatment, barring the collargol, was used.—*Le progrès médical*, 1904, No. 33, p. 105.

**The Therapeutic Action of Radium.**—MM. RAYMOND and ZIMMERN have investigated the analgesic action of this substance in affections of the nervous system. In tabes particularly was the influence of the radium noticeable. A series of patients affected with lightning pains, gastric crises, etc., received quick relief after the application of the rays.—*Revue de thérapeutique*, 1904, No. 16, p. 565.

**Stypticin.**—DR. M. FREUND reports on stypticin as being useful in the hemorrhages of the menopause; in the hemorrhages due to lack of involution after abortion or labor; in secondary hemorrhages resulting from diseased adnexa without disease of the uterus itself; in the congestive hemorrhages of young girls without pathological lesion; in myomata; in the hemorrhages of pregnancy. The drug is also of value in hæmoptysis and in bleeding from the rectum and bladder. It may be given in doses of  $1\frac{1}{2}$  grains, four or five times a day.—*Therapeutische Monatshefte*, 1904, No. 8, p. 413.

**Iodine in the Local Treatment of Uterine Conditions.**—DR. L. AMMOND states that iodine locally applied to the uterus has the great

advantage over other antiseptics of non-toxicity. It is especially useful as an intrauterine injection in puerperal sepsis. The author suggests the following formula: iodine 3 parts; potassium iodide, 6 parts; distilled water, to 1000 parts. When injections are not effectual, the author advocates curettage, after which the uterus is swabbed out with a bit of cotton, previously dipped in tincture of iodine.—*Journal de médecine et de chirurgie pratiques*, 1904, No. 16, p. 625.

**The Treatment of Infantile Eczema.**—DR. G. CLENET considers this a form of autointoxication due to disordered digestive action, and consequently the first indication is to attempt to regulate the gastrointestinal tract. If the child is breast-fed, feedings should be at a definite time and for a definite period. Bottle-fed children should be given properly modified milk. Older children should be fed chiefly on milk, with a limited amount of eggs and vegetables. If any meat is given, white meat is to be preferred. No tea, coffee, or alcohol should be allowed. The bowels must be kept regular. Arthritic infants should be given alkalis; scrofulous ones cod-liver oil, iron, or calcium glycerophosphate. In the sluggish eczema of children over five years arsenic may be administered. In cases which resist dietetic and internal treatment local applications are necessary. First the skin must be made as aseptic as possible by means of mild and non-irritating antiseptics or preferably by boiled water. The affected parts should be washed with cotton swabs—which must be thrown away after once being used—dipped in the solution. This is to be done several times a day and is to be followed by a dressing. If crusts are present they may be loosened by a poultice of potato starch, and later, if the area is not large, powders should be applied. On the scalp sterile oil containing a little salicylic acid is useful. Bathing is usually contraindicated. Before using ointments, powders and solutions should be tried, and when these latter have initiated the treatment, ointment of salicylic acid, sulphur, tar, or oil of cade are indicated. In oily and impetigenous eczemas dressings of silver nitrate have a favorable action; later tar or salicylic acid should be used. Finally, in children who resist the above treatments, weak pastes of pyrogallol or ehrysophanic acid may be tried.—*Revue française de médecine et de chirurgie*, 1904, No. 32, p. 765.

**Poisoning by Orthoform.**—M. BARDET, before the *Société de thérapeutique*, confirms the fact that ointments and liniments made with this substance are especially dangerous. He reports the case of a patient affected with itching of the legs for whom a 10 per cent. orthoform and vaselin ointment was prescribed. A pruriginous eruption appeared upon every part of the leg which the ointment had touched. At the same time the hands were the seat of a vesicular eruption, especially marked upon the right forefinger, with which the application had been made. On this finger the eruption was an actual and extremely painful zone. This lasted more than eight days and was followed by desquamation. The cutaneous manifestations were accompanied by general malaise and digestive disturbance lasting three days. The patient had previously suffered a like accident due to the same cause. Wet dressings relieved the symptoms. The case goes to show that orthoform ointments should be used with great care.

The powder seems unlikely to cause trouble. The author suggests that anæsthesine, which has like properties, be substituted for orthoform in ointments.—*Journal de médecine et de chirurgie*, 1904, No. 15, p. 589.

**The Treatment of Whooping-cough.**—DR. L. ITZKOWITZ uses in the treatment of pertussis vapor from the following mixture: naphtalin, 180 parts; powdered camphor, 20 parts; essence of eucalyptus and terebinthine, of each 3 parts. This preparation is mixed with boiling water, and the patient is so placed that he breathes its vapor for one hour a day. Of 15 early cases treated thus, a rapid diminution in the number and intensity of the attacks was noticed. Mild cases were cured in three to four weeks; severe ones in four to six weeks. Cases without complications received no other treatment, except proper diet and hygiene; no bad effects following the inhalations were noted.—*Allgemeine Wiener medicinische Zeitung*, 1904, No. 30, p. 337.

**Unguentum Crede in Ophthalmic Lesions.**—DR. W. FEILCHENFEL has treated about 200 cases of various kinds with, as a rule, very excellent results. It appears that the ointment is especially useful in infectious conditions in and about the eyes, and it is especially adaptable to the needs of the general practitioner. In severe cases it may be used pure, while in milder conditions it may be diluted 1 : 2 or 1 : 3 with vaselin. It is to be rubbed into the lining of the lids several times a day with a glass rod or smeared about the eye, as the case may be. The ointment should not be used in phlyctenular inflammations, nor in acute parenchymatous keratitis. Among the lesions successfully treated were phlegmons of the tear sac, gonorrhœal dacryocystitis, hordeolum, abscesses of the lids, purulent conjunctivitis, serous iritis, tracheoma (after expression of the cysts), and corneal ulcer.—*Therapeutische Monatshefte*, 1904, No. 9, p. 455.

## PEDIATRICS.

UNDER THE CHARGE OF

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AND

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**Gonorrhœal Salpingitis in Young Children.**—Two cases of this rather rare condition are reported in the *British Journal of Children's Diseases*, October, 1904, one by LEONARD A. BIDWELL, the other by GEORGE CARPENTER. Bidwell's case occurred in a girl of six years. With a purulent discharge from the vulva there was some superficial ulceration inside the vulva extending toward the meatus, pain after

micturition, and blood with the urine, but no enlargement of the inguinal glands. A few days later the child presented a painful swelling in the right foot, with redness and œdema over the flexor tendon sheath and pain on movement. The temperature was 102°. Incision on the following day evacuated some clear fluid from the tendon sheath. Examination at the same time showed pus issuing from the uterus. Gonococci were found in considerable numbers. About two weeks later, on account of the development of an abdominal swelling to the right of the median line in the hypogastric region, with evidences of a localized peritonitis, cœliotomy was made, and both tubes were found to be full of pus. They were removed, after ligature, close to the uterus, but the ovaries were left. The patient was rather ill for the first few days, but finally made an uneventful recovery and went home. The discharge, however, did not completely cease, and gonococci were still present. The child was readmitted and dilatation and curettement were done, with prompt recovery. Referring to the rarity of gonorrhœal salpingitis at such an early age, the author believes that its course is more acute than in adults. It is interesting to note that the discharge did not cease after salpingectomy, but persisted until the uterus had been curetted. Bidwell suggests that in cases of gonorrhœa in which the uterus has become infected, dilatation and curettement should be done, in order to prevent, if possible, further extension to the tubes.

CARPENTER's patient was only three and one-half years old. She had had a vaginal discharge of six weeks' duration, with pain in the lower part of the abdomen, and frequent micturition. The pus from the vulva contained numerous gonococci. Bimanual palpation of the pelvic viscera, with one finger in the rectum, showed involvement of the appendages. On the right side there was an irregularly-shaped elastic tumor attached to the uterus at the upper part, with its free extremity movable. On the left side the Fallopian tube apparently ended in fusiform swelling, which was attached to the side of the pelvis, and was probably an enlargement of the fimbriated extremity. About a month later the conditions had changed considerably. The left ovary and tube were of natural size, but the right tube was decidedly enlarged and terminated in a very elastic tumor half an inch or more in diameter. The uterus was normal to the touch, and all parts were freely movable. The vaginal discharge continued. About a month later the tube and ovary on the left were unchanged, but considerable improvement had taken place on the right side. The case is recorded as an example of the value of bimanual examination of the genitalia of young children, and as showing that in some cases at least these conditions tend to spontaneous recovery. Carpenter believes that sterility in adult life may result from such complications in infancy, and quotes the opinion of Marx, that these infantile inflammations are apt to commence afresh at puberty and often are the real cause of pelvic inflammations of newly married women hitherto frequently credited to the husband.

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**Pathogeny of Certain Diphtheritic Paralyses.**—M. E. RIST, chief of the laboratory of the Hôpital Trousseau (*Revue mensuelle des maladies de l'enfance*, September, 1904, p. 391), offers a valuable contribution to the discussion touching the true nature of post-diphtheritic paralysis. Most pathologists admit that in post-diphtheritic paralysis there are coincident lesions of the cord and of the nerves, some holding,



however, that these lesions are simultaneous and independent; others that the central lesions are primary and the peripheral are secondary; while others believe that the central lesions are secondary to the peripheral. Interesting as these findings are, they do not explain why these paralyses are produced, despite the early employment of anti-diphtheritic serum. In fact, it is the general opinion that such paralyses are more frequent since the introduction of the serum treatment, though this is probably explained by the fact that many cases are now saved which would have died in the pre-antitoxin period before paralytic symptoms could develop.

In this discussion it is important to note that exclusive reference is made to the late or so-called post-diphtheritic paralyses. The early paralyses are due to the soluble toxin in the blood and are a part of the picture of diphtheritic toxæmia, both clinical and experimental. They are exceptional since the widespread use of antitoxic serum early in the disease. The late paralyses appear in from eight to thirty or forty days after the end of the acute period of the disease, when all signs of local inflammation have disappeared and the mucous membrane of the pharynx is completely clean. As Mya has most forcibly insisted, these paralyses generally follow in the cases which have been characterized by a high degree of toxicity, and especially in those in which a more or less marked degree of albuminuria has been noted; and to these Rist adds the cases which have shown an abundant formation of false membrane. The interpretation of these cases is difficult. Mya has shown (*La pédiatrie*, vol. vii., fasc. 1, January, 1899) that there is no relationship between them and the experimental diphtheritic intoxication in the guinea-pig, in which the paralyses coincide with the general symptoms of the acute intoxication. In man, on the contrary, the clinical picture of post-diphtheritic paralysis is very clear, and experimentation with animals hitherto has never succeeded in reproducing it. Beginning with the uvula in the tonsillar cases or in the intrinsic muscles of the larynx in the primary croup cases, it may remain localized here in the milder cases or, in the more severe, spread progressively to groups of muscles which have their nerve centres in the medulla, or are innervated by nerves which have a common origin with those of the muscles of the pharynx or larynx, and finally to the extremities. Mya has pointed out that in the complete picture of post-diphtheritic paralysis there is a state of generalized muscular asthenia, not a true paralysis in the sense of an absolute loss of voluntary muscular innervation; the child presents a flaccidity, a diffuse muscular hypotonus, associated generally with abolition of tendinous reflexes, but is able to execute, in limited degree, a certain number of more or less co-ordinated and complex movements. The state of the muscles of the limbs and trunk reproduces very closely the clinical picture of the disease of Erb-Goldflamm.

As Luisada and Pacchioni had previously found, Mya has demonstrated that the diphtheritic toxin, like that of tetanus, is capable of propagating itself along the nerves to the cord, but he has also found that in immunized animals not the slightest motor disturbance has been produced by similar experiments, even when large doses of a more active toxin were used. Why then should not the use of antitoxin, even in massive doses, prevent the occurrence of late paralyses in man?

Rist believes that part of the truth may be found in Mya's hypothesis that there may be besides the soluble toxin another toxin of endogenous

formation, which is active by direct contact with the nervous system of the patient in whom it is formed, but inactive in the guinea-pig when introduced subcutaneously or intraperitoneally.

Rist's experiments have been directed to a study of the toxic properties of the bacillary bodies freed as much as possible from their soluble toxin. Emulsions of bacilli were injected into the peritonea of guinea-pigs and the veins of rabbits. The effects obtained were decidedly interesting. The animals resisted doses of 1 to 2 egm. injected intraperitoneally, but after the injection of 5 egm. or more they died, almost always after a period varying from twelve to twenty-one days. In some cases there was only a progressive wasting, leading to death by cachexia; in others there was pseudomembranous peritonitis, myocarditis, or nephritis; while others presented paralyses. These effects were produced in all the cases, despite the use of a considerable dose of antitoxic serum. The paralytic phenomena appeared gradually, and, in common with those observed clinically in man, were variable and incomplete. In the paralysis affecting the hind legs, which was the most frequent, the animal was inert, lying upon the belly, the two hind legs remaining in abduction stretched out upon the ground; when, however, it was actively stimulated, the animal struggled to its feet as if to run and then dropped down again into the position already described. These paralyses lasted several weeks if the dose had not been too strong; death occurred from paralysis of respiratory muscles after a larger dose of the poison.

These experiments prove, to the author's mind, that there exists in the bacillary protoplasm a substance manifestly toxic, diffusing slowly and slow in its action. This endotoxin differs from the soluble toxin, against which the serum-producer is immunized. It does not yield to the antagonistic properties of this serum, even in large dose. Does the existence of this endotoxin explain the resistance offered by certain symptoms in man to the therapeutic action of the serum? Rist believes that it does. Post-diphtheritic paralyses come on slowly in patients who have had abundant false membrane, probably very rich in bacterial elements. It is quite possible that the poison of these elements is propagated along the nerves. But whatever be the mode of propagation, the important fact is that it is not arrested by the antitoxin and can exercise its injurious influence at a time when the diphtheritic infection has disappeared.

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**A Case of Intussusception with Cure by Sloughing.**—IRVING M. SNOW (*Archives of Pediatrics*, July, 1904) reports a case of intussusception in which the invaginated gut became gangrenous and protruded from the anus.

The child, aged seven months, had the symptoms of ileocolitis, which ran a subacute course of sixteen days, when a protruding mass of necrotic tissue presented at the rectum. The gangrenous gut was ligated and the stump pushed back into the rectum. The patient passed gas and fecal matter daily. It was impossible to tell whether the specimen was a large or small intestine, so extensive was the necrosis. The patient made a perfect recovery. Spontaneous cure by the discharge of the intussusception is exceedingly rare in a baby under one year, there being but four other cases reported.

## OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE; PROFESSOR OF OBSTETRICS AND DISEASES OF INFANCY IN THE PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF DISEASES OF CHILDREN IN THE WOMAN'S MEDICAL COLLEGE; VISITING OBSTETRICIAN TO THE PHILADELPHIA HOSPITAL, ETC.

The Mechanism and Treatment of Recent Lacerations of the Pelvic Floor.—HENGGE (*Monatsschrift für Geburtshülfe und Gynäkologie*, 1904, Band xx., Heft 2) draws attention to lacerations in the perineum and pelvic floor which result from a separation of the vagina from the surrounding and underlying connective tissue. In many of these cases he believes that efforts to protect the perineum and pelvic floor indirectly bring about laceration by preventing the rapid and easy expulsion of the head. He also draws attention to the fact that occasionally severe hemorrhage complicates such lacerations. He believes that whatever the variety of laceration its only treatment is immediate suture. In 66 per cent. he obtained primary union, which was complete, and in the other cases partial union by the formation of scar tissue which was practically complete occurred. The morbidity of his clinic is a high one, because cases are extensively utilized for teaching. The use of rubber gloves, although faithfully carried out, has not especially reduced the morbidity. He has tried a procedure recommended by Zweifel, of thoroughly cleansing the vulva with sterile dry cotton about an hour after the expulsion of the placenta. He uses vaginal douches for offensive vaginal discharges only. In patients who had tears of the pelvic floor and perineum closed by suture a morbidity of 20 per cent. occurred—that is, in these patients a rise of temperature to or above 100° occurred in 20 per cent. He observed, what was frequently seen by others, that a patient may have a severe septic infection, and lacerations which have been sutured may close by primary union. In these cases the septic infection occurs through the uterus, usually at the placental site, the septic poisoning entering the blood or lymphatics directly.

Acute Yellow Atrophy of the Liver in the Puerperal Period.—COHM (*Zentralblatt für Gynäkologie*, 1904, No. 34) reports the case of a patient in the Breslau clinic who, five days after spontaneous parturition, was taken with high fever and chills. The uterus was thoroughly washed out, and collargol was given by intravenous injection without result. Jaundice developed, and the patient finally made a somewhat tedious recovery.

She left the hospital, and three days afterward her husband reported that severe jaundice was present and that the patient was highly delirious. She was admitted to the medical wards of the hospital, where she soon died.

Upon autopsy the liver was extraordinarily diminished in size. It

was bright yellow in color with reddish areas, and the spleen was not enlarged.

Of especial interest was the condition of the pelvic vessels. The right spermatic vein was filled solidly by discolored grayish-yellow masses. The inferior vena cava as far as the left renal vein was filled with an organized yellowish-black material. Both hypogastric veins were also occluded.

So far as the pathology of the case is concerned, it seems most probable that an infection of the pelvic bloodvessels was the immediate cause of the condition in the liver.

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**Vaginal Section for Eclampsia.**—In the *Zentralblatt für Gynäkologie*, 1904, No. 34, MALY reports the case of a multipara who had had toxæmia and eclampsia in some of her preceding confinements. On admission to the hospital the cervix was undilated, the patient comatose, having had convulsions. Operation was performed by grasping the cervix on the right and left side with tenaculum forceps, pulling strongly downward, making a transverse incision across the junction of the vagina with the cervix and pushing the bladder upward and backward. The anterior wall of the uterus was then opened above the internal os without opening the peritoneum. The membranes were ruptured, and the child was delivered by version and extraction. Some hemorrhage occurred, which immediately ceased when the placenta was delivered, and the uterus was packed with gauze. The cervix was closed with five catgut stitches and the transverse incision across the vagina with six. The space between the bladder and the uterus was drained by a small wick of gauze. The patient made an uninterrupted recovery.

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**The Effect of Childbearing on Fibroid Tumors of the Uterus.**—In the *Journal of Obstetrics and Gynecology of the British Empire*, August, 1904, DAKIN contributes a paper giving the result of his observations upon fibroids as affected by pregnancy, labor, and the puerperal period.

It is well known that fibroids grow during pregnancy. It is uncertain as to whether growth is most active in the earlier or later months. Such growth is usually a true hypertrophy, resembling that of the uterine muscle, while in some cases the increase within the tumor is due to œdema. The myoma cells increase much more largely than the muscular cells proper in most of these cases.

Fibroids frequently become œdematous during pregnancy, their spaces filled with serum or with brownish fluid containing red blood corpuscles and lymph cells. Extravasations of blood sometimes occur and are accompanied by considerable pain. If pus forms pain is increased, while œdema only gives rise to little or no pain. The softening brought about by œdema often permits spontaneous labor to occur by allowing the child to compress the tumor during parturition.

Fibroids rarely become necrotic during pregnancy, but cases sometimes occur in which the tumor breaks down in the centre, peritonitic adhesions sometimes form, and may cause incarceration and abortion.

If the uterus rises in the pelvis suddenly, dangerous hemorrhage may follow.

During pregnancy fibroids almost invariably become flattened. This is the result of pressure, increased area of the uterine surface

and the adaptability of the softening tumor to its widening base. After labor the fibroid again resumes its prominent shape.

In the great majority of cases the fibroid in the later months of pregnancy so changes its location as to leave the pelvic canal free for the passage of the foetus. Remarkable examples of this are reported in cases where the tumor filling the whole of the true pelvis has risen spontaneously out of the pelvis, and normal labor has occurred. The pedicle of a subserous fibroid occasionally undergoes torsion during pregnancy, followed by peritonitis and interstitial hemorrhage.

When fibroids are situated in the lower portion of the uterus and fail to rise above the pelvic brim they are subjected to mechanical violence during labor.

Dakin describes the case of a patient who had a fibroid growth below the pelvic brim attached as low as the internal os. Labor was induced at eight months, and a difficult delivery effected by forceps, followed by the death of the child. The tumor remained, and the mother had two abortions afterward, followed by a fourth pregnancy. In this a fibroid the size of an orange was present at the left cornu. On the right side of the uterus just above the brim was a fibroid mass two or three inches in thickness. As pregnancy advanced both of these tumors became softer and much smaller. Labor was normal. After delivery the fibroids were more plainly felt, but gave rise to no complications. Dakin cites the records of 5500 patients in whose deliveries fibroid tumors caused no obstruction whatever to labor.

During labor fibroids usually are drawn upward as the child proceeds downward. In this change there is some possibility of intraperitoneal hemorrhage if vascular adhesions are torn. If the tumor is extensively damaged it may slough. Very rarely a fibroid which has suppurated during pregnancy has ruptured during labor with fatal result.

The expulsion of submucous fibroids and inversion of the uterus in cases of labor complicated by fibroids have also been observed.

During the puerperal period fibroids usually undergo involution along with the normal muscle fibres of the uterus. There are also well-established instances of fibroids disappearing after pregnancy. Fibroids usually decrease in size after labor by simple atrophy; occasionally cirrhotic and other degenerative changes occur.

Dakin reports two cases in which fibroids were expelled during the puerperal period. In one the tumor was forced out spontaneously four days after labor, and in the other the fibroid presented at the external os on the fifteenth day, and was removed. The tumors were about the size of an orange and considerably flattened.

In the writer's experience, a patient some weeks after the birth of a child was taken with hemorrhage and pain, the cause of which remained undetected. Her symptoms became so severe during the night that the nearest physician was summoned, who found a mass protruding in the vagina. He attempted to remove it, but increased the pain and hemorrhage. When the patient was sent to a hospital examination showed a fibroid as large as a medium-sized fist attached to the fundus by a narrow pedicle. The uterus was inverted. Although the tumor was easily removed and the uterus replaced, the patient died of shock.

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**The Cardiopathy of Uterine Fibromyoma.**—In the *Journal of Obstetrics and Gynecology of the British Empire*, August, 1904, WILSON con-

tributes a paper upon this subject which is of direct interest to obstetricians in view of the common occurrence of fibroid tumors in child-bearing women.

As regards the frequency of lesions of the heart in this class of patients, Williams reports in 211 women treated for myomata 8 unoperated patients; 3.8 per cent. died, and in 2 of these cases death was due to disease of the heart. In 22 autopsies in these cases, 14 on patients dying after operation, the heart was normal in 12. In the other 10 valvular disease, fatty degeneration, hypertrophy, and dilatation, atheroma, and diminutive size of the heart were found. Wilson gives the notes of 4 cases from the records of the Birmingham General Hospital, where a pathological condition of the heart or great vessels was present and confirmed by autopsy. These patients died after operation. He also adds notes of 6 other cases, many of which did not come to operation and who did not die, in whom disordered condition of the heart and great vessels or thyroid gland was present. In all, in 274 patients having fibroids, including polypi, 72 were so seriously affected by the tumor as to demand operation. Among these, 46 per cent. had some disordered condition of the heart.

Myomata may indirectly bring about disease of the heart by the excessive size of the tumor pressing upon the diaphragm and ribs, preventing expiration and oxygenation of the blood. The tumor may press upon the ureters and cause degeneration of the kidneys. Fibroids often produce chronic anæmia, which affects the heart muscle. The vasomotor nerves may be destroyed through the influence of the heart upon the nervous system. In some cases of uterine fibroid, hypertrophy of the heart occurs when the tumor has as yet attained only a moderate size. Large tumors make great demands upon the blood supply, and thus bring about hypertrophy of the heart. When a fibroid develops in a patient who has valvular heart disease, compensation often fails under the increased strain.

In the majority of these cases interstitial fibroids are found, submucous next in frequency, and rarely subperitoneal tumors. In some of the gravest cases the tumors are not very large. General hypertrophy of the uterus is sometimes present with the tumor.

In dealing with these cases the liability to disorders of the heart should be remembered. The use of ergot may greatly increase the cardiac strain, and must in many of these patients be omitted. When fibroids bring about a weakened condition of the patient they greatly increase the liability to sepsis and also to thrombosis and embolism.

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**Practical Antisepsis in Teaching Hospitals.**—In the *Zentralblatt für Gynäkologie*, 1904, No. 33, AHLFELD gives the result of twenty-three years' experience in the Marburg clinic. During this time 1000 medical students and 2000 midwives received instruction. The method of disinfecting the hands consists in the free use of soap and water, and also the employment of alcohol with vigorous brushing. During this time 7000 births occurred and 50,000 vaginal examinations were made.

One patient during a normal labor, during a movement of the bowels, introduced her uncleaned hand within the vagina to ascertain the progress of labor. She died of septic infection on the eighth day, and the method of infection was subsequently ascertained.

During this time there were 20 septic deaths in 7000 labors, a mor-

tality of 0.286 per cent.; 15 of these patients were examined only by the staff of the clinic. Gloves were not used. The 20 septic cases are divided into three groups: those infected before admission, death following Cæsarean section, and death following prolonged labor in contracted pelvis with the induction of labor.

Of the 20 patients 9 were infected before admission, 7 perished after Cæsarean operation, 7 showed a form of increasing septic infection after long-continued labor; 11 had fever during labor.

Ahlfeld calls attention to what he terms increasing septic infection. Such are cases of long-continued labor, in which the bacteria of the genital canal take on unusual virulence and the infection continues and increases throughout parturition and the puerperal state. Other obstetricians agree with him in this observation.

Regarding his Cæsarean cases, he has had 23 operations, with a mortality of 7. This has resulted from his effort to perform celiohysterotomy in infected cases where celiohysterectomy or the total removal of the uterus should have been done. One of his fatal cases was infected before the operation; another had occlusion of the intestine, and perished after operation. His comparatively bad results draw attention to the necessity for performing the operation early and for the wisdom of declining to operate in cases that have been exhausted in prolonged labor.

Of 5 patients who had increasing septic infection after prolonged labor, 3 had the induction of labor. These 3 deaths occurred in 300 operations for the induction of labor and in women who had had labor pains for seven, ten, and thirteen days, respectively.

Ahlfeld's paper draws attention to the fact that it is possible by strict antisepsis to conduct the clinical teaching of obstetrics with a low mortality rate. His observation regarding cumulative sepsis is a good one, and also his demonstration of the danger of Cæsarean operation in exhausted labor.

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## GYNECOLOGY.

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UNDER THE CHARGE OF

HENRY C. COE, M.D.,  
OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D

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**Etiology of Cancer.**—LUTAUD (*Rev. prat. d'obstétrique et de gyn.*, 1904, No. 5) concludes his studies on this subject with a statement of his belief that cancer is not of constitutional origin and that thus far there has not been sufficient evidence to prove that it is inoculable or contagious. It always has a local origin, due to abnormal cell proliferation, the initial stage being almost identical with that observed in the formation of benign neoplasms.

The gravity of the prognosis in cancer is due to the absence of encapsulation and the involvement of the adjacent lymphatics. Leukæmia seems to favor the rapid development and dissemination of cancer. The practical inference from these facts is that if the surgeon is able to operate in the incipient stage of the disease a cure should be obtained. The writer concludes with an urgent plea against the popular idea that cancer is a disease of constitutional origin, since this undoubtedly prevents many patients from submitting to an early operation.

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**Treatment of Hemorrhagic Cystitis.**—FOLLY (*La gynécologie*, 1904, No. 5) describes a method of treatment which he has adopted successfully in the more severe forms of inflammation at the neck of the bladder in which hemorrhage is a constant symptom. He injects into a solution containing from one to two drachms of laudanum and half an ounce of antipyrin in a quart of sterile water.

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**Combined Cancer and Tuberculosis of the Uterus.**—WALLART (*Zeitschrift für Geb. u. Gyn.*, Band I., Heft 2) describes three cases of this rare condition, adding an exhaustive review of the literature. He agrees with Lubarsch and Naegeli that in certain cases tuberculosis of the uterus (especially of the cervix) may favor the development of cancer, although he admits with Stein that there is probably also a predisposition to the latter disease. The writer believes that the combination of these two diseases is more common than is usually supposed, as would be shown by a more careful microscopic study of specimens.

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**Lipoma Fibromatosum Uteri.**—SEYDEL (*Zeitschrift für Geb. u. Gyn.*, Band I., Heft 2) describes at length an interesting specimen and tabulates ten other cases, some of which were pure lipomata, while other tumors contained fibromuscular tissue.

Reviewing the different theories as to the origin of these mixed neoplasms, the writer offers the view that they are due to fatty degeneration of connective tissue or muscle elements, and holds, with Merkel and Knox, that they are explained by the inclusion of lipoblasts in the uterus in embryonic life.

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**The Curability of Cancer.**—LOMER (*Zeitschrift für Geb. u. Gyn.*, Band I., Heft 2) concludes an extended article on this subject with the statement that the repeated curettement and cauterization of cases of inoperable carcinoma may result in such an improvement of the local condition that a successful radical operation may subsequently be practicable. Due credit is given to the pioneer work of American gynecologists, notably Byrne, Baker, and Reamy, who reported 213 operations for advanced carcinoma of the cervix, with 140 patients free from recurrence at the end of five years (1).

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**Dissecting Metritis Associated with Diabetes.**—LIEPMANN (*Archiv für Gynäkologie*, Band lxx., Heft 2) reports three rare cases in which he regards diabetes as the principal etiological factor, and quotes in this connection an autopsy by Israel in a diabetic subject where both ovaries were found to be necrotic without any discoverable cause for this condition. The direct relation between glycosuria and necrotic



processes in the pulmonary and abdominal viscera (especially the pancreas) is well known.

**Lymphatic Invasion in Cancer of the Uterus.**—OLTRAMARE (*Annales de gynécologie et d'obstétrique*, 1904, No. 5) concludes that extension of cancer of the cervix to the body of the uterus is rare, and is observed only in advanced cases, and that this more often occurs by direct continuity than through the lymphatics. The latter are only likely to become channels of infection after the vessels at the bases of the broad ligaments have become thrombosed, so that a reflux of the lymph current occurs.

In cancer of the body of the uterus the lymphatics are generally involved later in the course of the disease, after the broad ligaments, adnexa, and peritoneum have become affected. The iliac, lumbar, and less often the inguinal nodes, are thus involved, and, more rarely still, those adjacent to the cervix. Visceral metastases, especially hepatic, are rarely observed, and are more likely to be due to extension from the peritoneum than through the vessels.

MANTEUFEL (*Beiträge zur Geb. u. Gyn.*, Band viii., Heft 2) in 33 specimens of cancerous uteri removed by abdominal section at the Halle clinic, found accompanying lymph nodes in 26 cases; 23 of these were examined microscopically, but metastases were demonstrable in only nine instances (27.3 per cent.).

The writer concludes that the palpation of enlarged glands in cases of cancer of the uterus by no means proves that they are cancerous, while, on the other hand, impalpable nodes may be found to be the seat of metastasis. The stage of the disease is no criterion as to the probability of lymphatic invasion.

The writer also notes the interesting fact that cancerous nodes may undergo spontaneous cure (!), though he admits that they are usually the cause of recurrence. He is, however, strongly in favor of the radical abdominal operation, though in the cases reported the immediate mortality was 21.2 per cent.

**Gonorrhœal Peritonitis in Children.**—VARIOT (*Gazette des hôpitaux*, March 8, 1904) reports the cases of two sisters, aged twelve and ten years, who were attacked with a purulent vulvitis, the discharge containing gonococci. The origin was obscure, but the elder girl was affected first and contaminated the younger, who occupied the same bed. Two days later they developed peritonitis, which gradually subsided, without operation. Appendicitis was suspected. As there was no evidence of accompanying tubal trouble, it was inferred that the infection was carried by the lymphatics. The writer calls attention to the usual mild course of gonorrhœal peritonitis, though fatal cases have been reported.

**Malignant Tendency of Ovarian Cysts.**—CERNE (*La gynécologie*, 1904, No. 4) calls attention to the fact that ovarian cystomata, like all neoplasms of epithelial origin, are to be regarded with suspicion, since they may at any time undergo malignant degeneration, especially the papillary variety. He estimates the malignancy of cystomata of the ovary as high as 12 or 15 per cent. Barnsby (*ibid.*) places the average much higher (56.25 per cent.).

**Multiple Nævi as a Sign of Malignancy in Pelvic Tumors.**—DENUCE (*La gynécologie*, 1904, No. 4) calls attention to Trélat's observation on the presence of multiple nævi of the skin in the neighborhood of a cancerous breast, and states that he has observed the same phenomena in connection with malignant tumors of the pelvis and abdomen, especially ovarian. He says that they are found in the skin over the seat of the neoplasm, and constitute a probable sign of its malignant character. Reference is made to similar observations by German writers.

**Reflex Muscular Spasms in Genital Troubles.**—GASTON (*La gynécologie*, 1904, No. 4) has noted certain muscular spasms of the arm, leg, and head on percussing the patella tendon in certain neurasthenic females, rarely in males. This reflex, which he calls the frog reflex (*réflexe ranien*), from the resemblance of the movements to those of a decapitated frog when the sciatic nerve is stimulated, are observed in women after hysterectomy and oöphorectomy, also in those suffering from unsatisfied sexual desire.

**Explorative Hysterotomy.**—Under this term BASTIAN (*Revue méd. de la Suisse romande, La gynécologie*, 1904, No. 4) commends a more thorough method of exploring the uterine cavity than is afforded by the usual dilatation and palpation. Under strict aseptic precautions the anterior vaginal fornix is incised and the bladder is separated by blunt dissection in the usual manner. The cervix is then split upward into the uterine cavity, so that the latter can be thoroughly examined and any operation performed without opening the peritoneal cavity. The uterine wound is then sutured with catgut, and the vaginal with silkworm-gut. If sufficient room is not obtained the posterior lip may also be incised, although this is rarely necessary.

**Infection from the Mouth of the Surgeon.**—MENDEZ DE LEON (*La gynécologie*, 1904, No. 4) emphasizes the fact that sufficient attention has not been paid to the danger of infecting the abdominal cavity by the surgeon who talks during an operation. In order to test this point he repeated his remarks during a previous laparotomy, speaking into a sterilized box. Cultures from the air in this box showed both streptococci and staphylococci, while a single drop of the operator's saliva contained 140 different micro-organisms.

The writer recommends washing the mouth with an antiseptic solution before a clinical lecture and also the wearing of a mouth-mask.

**Necrosis of Fibromyoma after Palliative Treatment.**—KUBINYI (*Zentralblatt für Gynäkologie*, 1904, No. 24) reports the case of a primipara, aged forty-two years, with a multiple fibroid filling the lower abdomen and causing menorrhagia. Tincture of iodine was injected into the uterine cavity to check the bleeding. Two days later the patient had a chill, elevation of temperature, and severe pain. These symptoms subsided in a week, but the patient appeared to be septic, and it was inferred that the tumor had begun to necrose. On opening the abdomen fresh adhesions were found, and the fibroid presented a brownish appearance. Supravaginal amputation was performed, and it was found that there was a necrotic area on the endometrium, with thromboses in the vessels extending into the tumor.

In the discussion following the presentation of this case before a Hungarian medical society, Barsony called attention to the fact that there was probably a lesion of the uterine mucosa which allowed the entrance of infection, since tincture of iodine in itself was a powerful antiseptic. He had observed no bad effects after intrauterine injection of the drug unless it entered the tubes, or caused lesions of the mucosa.

[To the ordinary reader there is only one lesson to be derived from this case—not to use iodine at all under the conditions stated. We have recently operated in a case of ovarian abscess resulting from an intrauterine application of Monsell's solution within the cavity of a fibroid uterus, the patient having general infection and renal complications, from which she recovered only after a long illness. Lesions of the uterine mucosa covering a sessile submucous fibroid are fraught with more or less risk, even when made with the curette under strict aseptic precautions.—H. C. C.]

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## DERMATOLOGY.

UNDER THE CHARGE OF

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**Roentgen Rays in Cancerous and Skin Affections.**—J. H. BRAUTH (*New York and Philadelphia Medical Journal*, June 11, 1904) finds that in cancer the results of this method of treatment are variable, but that the deeper the cancer the greater the difficulty to conquer the disease; yet it has been the experience of the author that in nearly all the deeper seated cancers (especially of the mamma) the disease comes to a period of rest, further development being arrested for a time. Not one case of cancer of the breast receded to health under the rays alone, but a more or less doughy deposit remains as a dormant focus, which at any time may wake up into any degree of activity. In epithelioma, rodent ulcer, lupus, and some other diseases of the skin the rays "prove an almost certain remedy." A case of lupus is well illustrated by photographs.

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**Preliminary Notes Relative to Spark-gap Radiations.**—H. G. PIFFARD (*Journal of Cutaneous Diseases*, June, 1904) states that it was long ago determined that the radiations from a condenser spark contained a relatively larger proportion of ultra-violet than any other natural or artificial source, an observation first made use of therapeutically by Goerl, of Nuremberg, who employed aluminum terminals with four spark-gaps. Later Piffard introduced a lamp with iron terminals and three gaps, which bears his name. Up to a very recent date

physicists have declared that the cathode rays of the Crookes tube, being wholly absorbed by the glass, did not pass through it, but lately Oliver Lodge states positively that at least some of the rays do emerge, a view that Piffard has long held. Piffard puts forth the hypothesis that the rays affecting the electroscope are negative electrons (and not ultra-violet undulations), and that their velocity will be found to be much less than the cathode rays of the vacuum tube, and still less than the unimpeded *beta* rays of radium. In further confirmation of this hypothesis Piffard finds that the radiations from the condenser spark discharge the electroscope when carrying a positive charge, which would not be the case if they were purely ultra-violet undulations. Freund, referring to the period of latency that intervenes between the time of impact of the spectrum rays and the appearance of cutaneous reaction, lays down the law that this latent period varies inversely with the wave length of the impinging ray, or, as Piffard prefers to state it, varies directly with the frequency of the undulation. If this holds good as regards the velocity of electrons, it would lead us to expect cutaneous reaction to appear more promptly than with either the Crookes tube or with radium, and Piffard further anticipates that the character of the reaction will resemble that which follows the use of a "soft" *x*-ray tube. In testing these radiations all ideas of compression must be abandoned, and the skin rendered anæmic by adrenalin in the manner formerly proposed by Piffard.

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**Treatment of Tylosis Palmaris in Adults.**—TH. MEYER (*Dermatologische Zeitschrift*, May, 1904) recommends the "peeling cure" by means of Lassar's paste of naphthol, composed of  $\beta$ -naphthol, 10.0; precipitated sulphur, 40; vaselin and soft soap, of each 25, in combination with carbolyzed diacyton ointment, made of diacyton plaster and vaselin, equal parts, to which is added 2 per cent. of carbolic acid, washing with soap and water, massage, and the use of salicylic acid preparations. In a note in the same journal Lassar states that this treatment, attributed to him, is permanent in results.

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**One Hundred Attempts to Inoculate Alopecia Areata.**—L. JACQUET (*La presse méd.*, December 12, 1903) made the experiments, many of them inoculations, and gives some interesting data, but the result arrived at is that this disease is not inoculable in any of its varieties, and that the prophylactic measures recommended by some authors are entirely useless and unnecessary.

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**Bacilli in Syphilis.**—L. WAELSCH (*Archiv f. Derm. and Syph.*, January, 1904) investigates especially the micro-organism of v. Niessen, based upon a series of bacteriological investigations made in subjects of syphilis. A bacillus similar to that of v. Niessen was observed in the blood in twelve out of thirty-five cases of syphilis in the secondary stage. The author, however, concludes that its presence has no etiological relation with the disease. It is found in syphilis, but it is not the cause of the disease.

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**Psoriasis Arthropathy.**—DARIER (*Journal des praticiens*, 1903, No. 45; *Monatshefte für Praktische Dermatologie*, Band xxxviii., Heft 11) does not regard the association of psoriasis and arthropathy as

accidental, but as a well-characterized, tolerably frequent disease *sui generis*, the chief symptoms of which differ on the one hand from ordinary psoriasis, and, on the other, from all other forms of arthropathy. The eruption never occurs in small, round foci, but always in extensive plaques which are localized by preference in the axillæ, the cleft between the nates, and on the posterior surface of the scrotum, and are extraordinarily refractory to treatment. The arthropathy appears without any previous infectious disease; several joints are simultaneously affected; the course is rapid, and the final result is marked deformity. Cardiac sequelæ do not occur. Many cases resemble that form of gonorrhœal rheumatism which is localized upon the fingers. Investigation with the Roentgen rays has shown that the terminal phalanges of the fingers are completely absorbed, while the other phalanges are markedly rarefied. Osteophytes also occur, which may lead to ankyloses or luxation of the joints. The etiology of the disease is completely unknown. Neither local nor general treatment produces any effect.

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## OPHTHALMOLOGY.

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UNDER THE CHARGE OF

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**Empyema of the Frontal Sinus; Orbital Complications Treated by Superheated Steam.**—DENNIS (*Archives of Ophthalmology*, July, 1904) reports a case treated by the method advocated by Dr. Golovine, of Moscow (*Archives of Ophthalmology*, vol. xxvii.). The patient, a man, aged fifty-one years, had severe cellulitis of the right orbit, the eyelid was closed, and the ball pushed forward, downward, and inward; fluctuation above. A free opening was made in the upper outer one-third of the orbit, resulting in a free discharge of thick, offensive pus. A small roughened area of bone was found, also an opening leading into an unusually large frontal sinus. Fluids passed into this opening and discharged slowly into the nostril, but the sinus could not be thoroughly emptied in this way. The opening into the sinus was kept open and the thick mucoid discharge washed out. By the removal of numerous polypi and the tip of a thickened middle turbinate an effort was made to establish a permanent opening into the nostril. After thorough irrigation three times daily for six weeks there was no diminution in the thick mucopurulent discharge. An opening was then made under ether into the frontal sinus, which was found to be 32 mm. in its transverse diameter. The mucous membrane was curetted as thoroughly as possible, and a drainage-tube was passed from the sinus into the nose. The opening into the orbit was allowed to close, and irrigation

was kept up through the external opening with free drainage into the nose. After three months of this treatment the discharge stopped. Four months later the patient returned with profuse mucopurulent discharge into the nostril. Irrigation through the nostril had no effect in lessening the discharge.

Obliteration of the sinus was then determined upon, and, as chiseling the anterior portion of the sinus would leave a large scar, the method of Golovine was chosen. Under anaesthesia a new opening was made through the old scar, and superheated steam was allowed to flow into the sinus. Three applications were made, the total time being one minute. The sinus was lightly packed with iodoform gauze. There was no reaction following the operation. The packing was removed daily and the cavity irrigated with 50 per cent. peroxide of hydrogen.

The patient was under observation for five and one-half years after the operation. There was no return of the trouble, no exophthalmus, and but little disfigurement, the scar having the appearance of a small bullet wound.

The writer advocates the use of this method in selected cases as being easy, safe, thorough, and, with proper precautions, leaving a minimum amount of disfigurement. It is not applicable to cases of necrosis or where the disease has extended to the brain. It may be used with advantage combined with radical operation.

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**Observations on the Prognostic and Diagnostic Value of Retinitis in Diabetes.**—NETTLESHIP (*Royal London Ophthalmological Hospital Reports*, June, 1904) believes that the presence of retinal changes in a person with diabetes does not point to the probability of early death with the same frequency as does the retinitis of chronic Bright's disease. In support of this view he gives the result of observations made upon 48 patients who had diabetic retinitis or retinal hemorrhage. The age of the patients ranged from forty-one to seventy-nine years; 38 of the 48 are known to have died; 9 died within twelve months of the discovery of the retinitis, and 11 others during the second year—*i. e.*, 19 died within two years of the retinitis being discovered. The remaining 18 died at periods varying between two and eight years, and to this number must be added 10 others who were living at dates varying from two to ten years from the retinitis. Thus 60 per cent. lived more than two years after the eye disease was found, and only about 20 per cent. died within one year. This is widely different from the history of ordinary renal retinitis (excluding pregnancy cases), in which among the author's own cases less than one-third lived two years after the retinitis, and nearly two-thirds succumbed within twelve months. The prognosis for life is, therefore, much better in the renal cases of all ages (excluding those caused by pregnancy).

In many of the diabetic cases the retinal degeneration (exudation and hemorrhage) increases either steadily or by repeated relapses, even when the general condition of the patient has improved. As regards improvement of vision, therefore, the prognosis in diabetic retinitis should be very guarded.

Since many of the subjects of diabetes also pass more or less albumin a doubt has been expressed as to whether the retinitis was not caused by coincident renal disease. Nettleship states that there appears to be

no ground for doubting that one-half to three quarters of the subjects of glycosuria in whom retinal complications occur die directly from their diabetes and not from any accompanying renal disease, and the presumption in these is that the ocular mischief is caused by the principal malady.

There is also direct evidence that diabetes alone can cause retinitis in cases where the urine is from beginning to end free from albumin.

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**Primary Chancre of the Conjunctiva and Interstitial Keratitis.**—COLLINS (*Royal London Ophth. Hospital Rep.*, June, 1904) reports a case of primary chancre of the left lower lid. Eight months after the appearance of the sore the left eye became the seat of interstitial keratitis. The writer refers to five other previously reported cases. In all these cases the keratitis was confined to the eye on which the primary lesion was situated. The association of these two rare affections in this group of cases would seem to imply more than a chance coincidence. It would suggest that the proximity of the primary lesion in syphilis to the eye predisposes it to become subsequently the seat of an interstitial keratitis. The fact that in each case the keratitis occurred in the eye on the side on which the chancre was situated and on that side only is further in keeping with this suggestion.

The writer also reports another case which is worthy of record, but which differs from the others in that the primary lesion was on the lip instead of the lid.

In these cases of interstitial keratitis coming on in acquired syphilis it is interesting to note the remarkable variation in the time which elapsed between the occurrence of the primary lesion and the onset of the ocular trouble. The shortest interval was five months, the longest ten years.

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**Amblyopia from Disease of the Optic Nerve (Retrobulbar Neuritis). Its Treatment by Hypodermic Injections of Strychnine.**—ROOSA (*Post-Graduate*, July, 1904) advocates the use of hypodermic injections of strychnine in increasing doses in the treatment of toxic amblyopias. He believes that the best results are achieved when the injections are made in the temporal region, although he was often obliged to make the injections in the arm, and in some cases no injections were used, but the strychnine was given internally. If this treatment is undertaken while the lesion is a retrobulbar neuritis, before atrophy has occurred, a cure is to be expected. Atrophy from syphilitic infection is incurable and is of spinal or cerebral origin, and not the result of a retrobulbar neuritis. The writer has found the treatment by strychnine effectual in purely neuritic cases only. When the disease is of spinal or cerebral origin strychnine offers no hope.

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**Foreign Bodies in the Eye and their Removal with the Electromagnet.**—MARPLE (*Medical Record*, June 25, 1904) records several cases, types of the various forms of injuries due to foreign bodies in the eye. He states, in conclusion, that an eye in which a piece of iron or steel is buried invariably deteriorates, and ultimately becomes blind if the foreign body is not removed, unless it becomes completely encapsulated. If the foreign body is in the anterior segment of the eye the Haab magnet is almost universally used, at least to get the particle into the anterior chamber.

The injury in the great majority of cases when it is in the anterior segment of the eye is not attended with a prolapse of the iris, and the occurrence of this complication makes it probable that the foreign body has not penetrated the globe. This symptom is not a reliable one in case the foreign body has made a large or irregular wound in the eye.

If the foreign body has penetrated into the vitreous or posterior part of the globe, localization either with the sideroscope or x-ray had better precede any attempt to extract it, especially if the lens is still transparent. After the particle has been localized it can be removed by way of the anterior chamber with the Haab magnet, or by opening directly into the sclera near where the particle has been located.

If the symptom of pain cannot be elicited with the Haab magnet this is to be interpreted as evidence that there is no foreign body in the eye; that it is enveloped, in recent cases, in a fibropurulent exudation, or a blood clot, or (in less recent cases) that it is firmly encapsulated, that it has passed entirely through the globe, and is lodged partly or wholly in the orbital tissues (double perforation).

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## HYGIENE AND PUBLIC HEALTH.

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UNDER THE CHARGE OF

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**The Chemical Constitution of Bacterial Cells and the Mode of Formation of Antitoxins.**—The chemical constitution of bacterial cells and the mode of formation of antitoxins in the body are subjects which to-day are commanding an enormous amount of scientific investigation. No contribution to the solution of the question of chemical composition has appeared which is more worthy of note than that of Professor V. C. VAUGHAN (*Journal of the American Medical Association*, September 3, 1904, p. 643). Various of his students have shown the presence of carbohydrates, nuclein bodies, proteids, and poisons in the cell substance of a number of species of bacteria, and lately he and Wheeler have succeeded in splitting off, by means of sodium alcoholate, highly poisonous groups from the cell substance of the colon, typhoid and anthrax bacilli, and with these groups they have produced neutralizing antibodies. Investigation of the colon toxin leads Vaughan to the conclusion that it is composed of a haptophore and a toxophore group, and he suspects that the toxin group is a neurin, the reasons being both chemical and physiological. The part of the colon cell substance which is soluble in water is non-poisonous, but it yields a hæmolysin and a group that splits up the hæmoglobin into hæmatin and a globulin. The split-off toxin, thrown into the peritoneal cavity of a guinea-pig, causes death, with no evidence of irritation of the peritoneum, within very few minutes; but when the sterile germ substance is introduced, the result is a hemorrhagic peritonitis, ending in death in from ten to twenty-four



hours. Vaughan believes that the colon bacillus is a definite chemical compound, in whose molecule has been demonstrated the existence of the following groups: nuelein, amido, diamido, monoamido, carbohydrate, toxie, hæmolytic, and hæmoglobin-splitting. Probably many other groups and subgroups also are present; and in all the groups are attached to one another, forming a highly complex molecule, which splits up on lines dependent upon the kind and amount of energy applied. Since the force which holds the several groups in the molecule varies in strength, some groups are split off more easily than others. The cells of the body are doubtless equally complicated in their chemical constitution, and Vaughan believes that the reaction between a bacterium and a body cell is as definitely chemical as that between sulphuric acid and calcium carbonate. If the chemism between a group of the one and a group of the other is greater than that which holds these groups in their respective molecules, a reaction takes place, the two groups form a new molecule, and the injury done to the bacillus or the cell depends upon the group that has been abstracted. Without such reaction, no body cell can be harmed by a bacillus molecule, but when such a reaction is possible it occurs much more rapidly if the group which forms the union is injected after being split off, rather than as a constituent part of the complex molecule. This is the reason why the toxin and the sterile cell substance produce their results after such differing intervals, the colon molecule requiring splitting up before the toxie group can become active. Still more rapid is the action when the free toxin is injected intravenously and thus reaches the cells of the respiratory centre more directly. Assuming this reaction between bacillus and cell to be true, the formation of antitoxins can be explained; and Vaughan offers an exceedingly simple, sensible, and reasonable explanation, which, briefly, is as follows: If the chemical attraction between the toxin group and a given group in the cell is stronger than that which holds these groups in their molecules, they unite and form a saturated, stable, new molecule which is not harmful. The cell is injured, but not destroyed, and it proceeds to repair itself by splitting off from the nutritive substances within the range of its chemism groups similar to that which it has lost; but splitting off more than it needs, the excess becomes the antitoxin of the blood serum. With the toxin in question, the fatal results are explained as follows: The toxin group has a special chemical affinity for the cells of the respiratory centre, which are not destroyed by the toxin, but a certain number of them are thrown out of commission, and if the number be great enough respiration ceases and the animal dies. This paper of Dr. Vaughan's is a very important and illuminating contribution to the literature of an exceedingly complicated subject, and his hypothesis of antitoxin formation appears to have a more substantial scientific basis than any other thus far advanced.

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**Transmission of Tuberculosis through Flies.**—Noticing the number of flies that flock about the cuspidors of phthisical patients, Dr. E. H. HAYWARD (*New York and Philadelphia Medical Journal*, October 1, 1904, p. 643) undertook a series of experiments with the common house fly and the blue-bottle fly to determine whether or not they may be an etiological factor in tuberculosis. Sputum in which the bacilli were known to be present was put into watch-glasses and covered with fine wire screens, on which the flies could rest and

feed through the meshes without soiling their feet and wings. Six hours afterward clean cover-glasses were introduced, and during the next three or four hours these became soiled with the flies' excrement. Examination showed tubercle bacilli on each one. That the vitality of the bacilli was not impaired was proved by making cultures of the feces on glycerin agar and obtaining growths of the organism, and also by injection of the feces, rubbed up with sterile water, into the peritoneal cavity of guinea-pigs, which developed tuberculosis. The author points out that through the agency of flies the bacilli may be carried from the sputum of one person and deposited upon the food of another, so that the passage from one person's lungs to another's alimentary canal may be accomplished within a few hours.

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**The Copper Sulphate Treatment of Water.**—During the few months that have elapsed since the publication of the results of experiments conducted by MOORE and KELLERMAN (*United States Department of Agriculture, Bureau of Plant Industry, Bulletin 64*), on the use of extremely dilute solutions of copper sulphate as an algacide in reservoirs and ponds overgrown with algæ and for destroying typhoid and cholera infection, many practical applications of the method have been made in various parts of the country, with results varying from complete success (against algæ) to utter failure. The authors gave warning, however, that each body of water should be studied separately as a distinct problem, and invited consultation in every case of intention to attempt treatment. Objection has been made in various quarters to the use of even so minute an amount as one part of copper sulphate in 5,000,000 of water, on account of possible ill-effects therefrom, although the daily ingestion of small amounts of that salt is held, rightly or wrongly, by most authorities to be free from danger to health. But it is asserted that within a very short time all traces of copper disappear from the solution. However this may be with some waters, it is not true with all, for it is the experience of the present writer and of probably many others that evidence of its presence may still be found some weeks after the treatment. It is said that the authorities of Elmira, N. Y., added not 1 part in 5,000,000, but 1 in 700,000, or about seven times as much, and that a litre of the water, taken thirty hours after treatment and concentrated by evaporation to a single cubic centimetre, yielded not the slightest trace of copper, it having been precipitated after performing its office. In this instance, it may be noted, there occurred complete destruction of the algæ and a diminution of more than 90 per cent. in the number of bacteria. In some cases, objection has been raised that, although the algæ are destroyed, the turbidity persists; but generally the killing of the algæ is followed by their rapid disintegration, with disappearance of turbidity. In other cases a more serious objection is that while certain species are destroyed far more easily than others, and although overgrowth by these may prevent the latter from undergoing extensive multiplication, the disappearance of the easily-destroyed species may remove the obstacles to and be followed by an overgrowth of an equally objectionable but more hardy species. With regard to the bactericidal power of colloidal solutions of copper, there are already many remonstrances that the original statements appear not to be justified. Among those who report against placing any reliance upon this form of treatment of public water supplies for the destruction of typhoid infection is

Professor John H. Long, of Northwestern University, who made an investigation of the subject in behalf of the Illinois State Board of Health. In a communication from Dr. J. A. Egan, the secretary of that board (*Journal of the American Medical Association*, October 15, 1904, p. 1157), Professor Long is quoted as saying: "While in sterilized water in contact with copper the death rate of typhoid bacilli is high, their persistence for two or three days, and the possible persistence for longer periods in larger amounts of water, render the method impracticable for use in rendering a suspicious water safe for household use." Attention is called to the fact that typhoid bacilli disappear from ordinary water in from one to ten days without treatment, and that, therefore, "the disappearance of the bacilli forty-eight hours after seeding in a copper vessel may be due not only to the action of the copper, but to the natural destruction of the bacilli in water."

**Pus and Bacteria in Milk.**—In 1900 it was pointed out by DR. D. H. BERGEY that a high cellular and bacterial content of milk appears to be associated with some inflammatory process within the udder. Since then DR. BERGEY (*University of Pennsylvania Medical Bulletin*, July-August, 1904) has studied the milk of several cows during an entire period of lactation, in order to obtain information concerning the relation of the period of lactation to the cellular and bacterial content. The milk of one of the cows selected for observation showed, previous to the preceding period of lactation, a slight amount of pus in association with staphylococci. That of Cow No. 2, examined for the first time after calving, showed no pus, but merely the normal leukocytic content, which is equivalent to the presence of not more than ten cells per field of a one-twelfth immersion lens. Cow No. 3 was suffering with contagious mammitis, and her milk after calving showed large amounts of yellow pus and very large numbers of streptococci. The milk of all three of these cows was examined at intervals of one or two months, until the close of the period of lactation, a period of nine months. The results of the investigation led to the following conclusions: 1. The occurrence of pus in cows' milk is probably always associated with the presence in the udder of some inflammatory reaction brought about by the presence of some of the ordinary pyogenic bacteria, especially of streptococci. 2. When a cow's udder has once become infected with the pyogenic bacteria, the disease tends to persist for a long time, probably extending over several periods of lactation. 3. Lactation has no causative influence *per se* upon the cellular and bacterial content of cows' milk, although it probably tends toward the aggravation of the disease when the udder is once infected. 4. Contagious mammitis, the "gelbe galt" of European writers, appears to be merely a severe form of mammitis due to a variety of streptococci, which, on account of its chromogenic properties, gives to the milk its peculiar golden-yellow color.

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COPIOUS WATER-DRINKING AND POLYURIA IN TYPHOID  
FEVER. A CONTRIBUTION TO TREATMENT.

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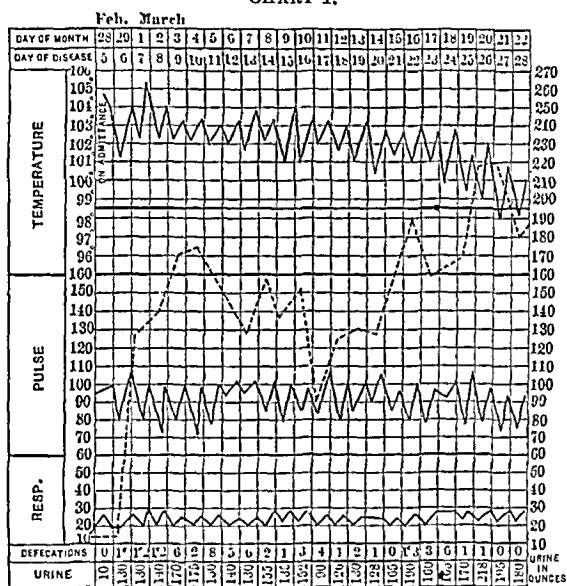
DURING the summer months of 1903, when, typhoid fever being unusually prevalent in Cleveland, the wards of the Lakeside Hospital contained many cases of this disease, an attempt was made, at first in the female ward alone, to give much larger quantities, than usual, of water to drink to the fever patients, to determine its effects on their comfort and condition. The free use of water internally is, of course, accepted as important in the treatment of typhoid fever; and it has been the custom in the hospital to see that a patient with this disease should have what was thought an abundant supply. In the nursing directions, three pints daily has been set as the least amount which such a patient should receive; and besides the water given by the nurse, a quart bowlful of ice-water with a bent-glass tube on a stand by the bed-side has enabled the individual to help himself with a minimum of exertion. The twenty-four-hour amount of urine, always measured and charted, has shown in most cases a daily record of from forty to fifty ounces during the time of the fever, and this has been taken as a fair index of sufficient fluid ingestion.

In trying to administer additional water it was soon found, with the efficient help of an admirable head-nurse, that without discomfort or special reluctance on the part of most patients, the unexpected and unusual amounts of from a gallon to a gallon and a half, or even more, could easily be taken. This was accomplished by giving four ounces of water every fifteen minutes during the waking hours, amounting to from eight to fourteen pints,



according to circumstances, in the twenty-four hours. In addition the ordinary patient received every two hours during the day, and once or twice at night, alternately six ounces of milk and six ounces of albumen-water, representing some three pints more of fluid. These large quantities, so given, were well borne. An occasional patient rebelled at first at the frequent dosage, but most took the water readily and some greedily, and the reluctant were, as a rule, soon persuaded that their comfort was enhanced thereby. The resulting diuresis was marked. The amount of urine passed in the twenty-four hours after admission in the average case was found to be about twenty ounces. After forty-eight hours, or by the end of the third day, with much uniformity in the abrupt response to

CHART I.



V., Med. No. 4231. The broken line shows the urine in ounces.

the copious water-drinking, as the charts show, there resulted a daily elimination of from eight to twelve pints, and even in some cases two gallons or more of urine; and the polyuria was readily kept near this level in an uncomplicated case during the febrile part of the illness. A daily urine flow of from 120 to 160 ounces was established and maintained with ease in the average case (Chart I.); 220 ounces and more were not unusual (Charts II. and III.), and in an occasional instance, like that of Annie M., Medical No. 3720 (Chart IV.), ten ounces were passed on the day of admission, to be succeeded on the third day by the enormous flow of 431 ounces, while the average elimination was 270 ounces.

The daily number of typhoid fever cases in the hospital at this time was from forty to fifty, and the nursing-staff was taxed to the utmost with the routine care of the patients, and especially with the great number of tub-baths required. In the ward, however, where this experiment in hydrotherapy was undertaken, the head-



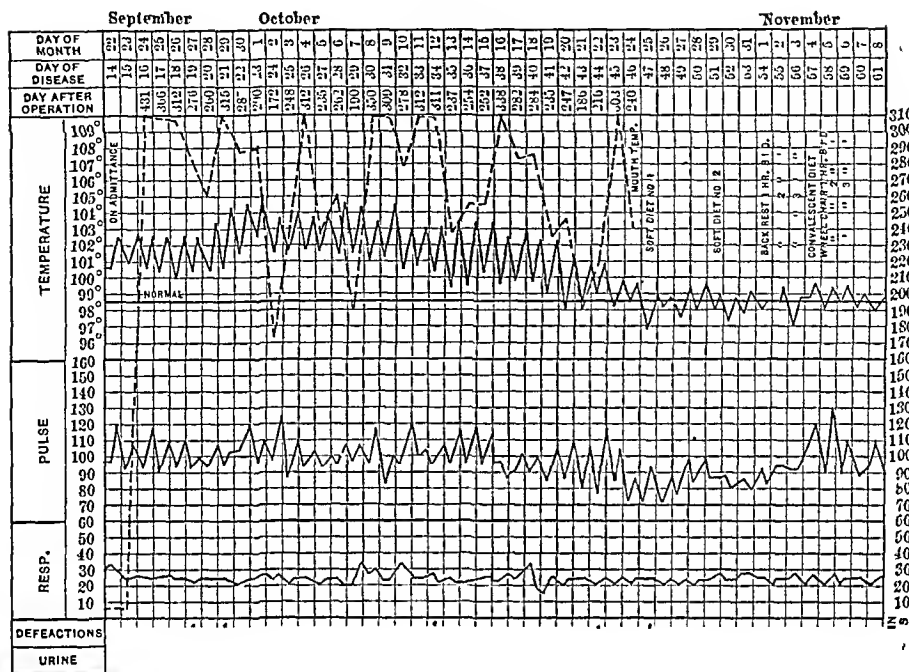
nurse was soon decided in her judgment that fewer baths were needed and that the total nursing care of the typhoid patients was less, in spite of the extra attention which the frequent administration of water and the increased use of urinals involved. In the bedside observation of this group of cases, the general comfort of the patients so treated seemed apparent. Headaches were not so troublesome, so that the familiar ice-bag was much less in evidence in the ward. Tongues and mouths kept noticeably clean and moist, and the toilet of the mouth cavity was a much simpler nursing task. Apathy, deafness, restlessness, nocturnal delirium and other nervous and toxæmic symptoms seemed less in evidence, hypnotics were not so often needed, nausea was unusual, and remissions in temperature appeared more frequent. Complications, minor and major, were few among the patients, and there were no deaths in this first small series, amounting to twenty cases, though the prevailing epidemic was of severe type, and the general mortality in the community and in the other wards of the hospital at the same time was large.

An additional year's experience, during which this element of treatment has been continued with more or less thoroughness in all the medical wards of the hospital and in the services of Dr. H. H. Powell, Dr. J. H. Lowman, and Dr. H. S. Upson (I am greatly indebted to these gentlemen for permission to utilize their cases), as well as of the writer, has seemed to confirm the early impression of its usefulness, and demonstrated that in all cases of typhoid fever, unless on admission profoundly toxic or with serious complications, or in the case of children who will not, as a rule, take water so often, this very abundant flow of urine can be secured with certainty in forty-eight hours and kept up during the illness. The method of administration first adopted of having the patient receive, when awake, four ounces of water every quarter of an hour, has been continued. Larger quantities at a time are less acceptable, and often not well tolerated, while small amounts, frequently given, are usually not unwelcome.

The urine in these cases when the daily amount exceeds a gallon, is extremely pale, with a specific gravity of from 1001 to 1005. With an elimination of more than 200 ounces, the specific gravity of the watery fluid is often below 1001. There was found to be a close approximation in the absence of diarrhœa or sweating, between the amount of fluid ingested and the quantity of urine eliminated. Thus in the case of K. (Chart III.), during ten days, 2664 ounces of fluid were given, while the quantity of urine passed was 2626 ounces, an average daily difference of some four ounces. On certain days the amount of urine passed would slightly exceed the liquid taken. When obvious perspiration was present, or several loose movements occurred, the disproportion was, of course, more marked.

In the case of B., Medical No. 4230, where the skin kept moist during most of the illness, 1358 ounces of fluid were given in six days and 844 ounces passed, a daily average of 226 ounces and 140

CHART IV.



ounces, respectively. Chart V. shows the effect of repeated hemorrhages upon the quantity of urine, with the subsequent stoppage of milk and restriction of water supply.

From June 1, 1903, when the treatment was begun in one of the wards, to October 1, 1904, 100 cases of typhoid fever have shown a daily urine flow of 100 ounces or more; in 56 of this number the amount has been between 100 and 160 ounces; in the other 44 cases, over 160 ounces. During this entire period of sixteen months, 308 cases have been in the hospital, but during the eight months since January 1, 1904, only 105 cases, the improvement in the Cleveland water supply having greatly lessened the frequency of the disease since April, 1904. And as it was not until February, 1904, that this method of water-giving became general in the medical wards, the 100 cases represent a more nearly consecutive series than the discrepancy in totals would indicate.

These cases have been carefully analyzed by Dr. Clarke, who, as resident physician, has had charge of most of them, as to their course, complications, and fatality, and contrasted with a series of 50 cases during the early part of the same period, in which there was no attempt to establish polyuria, and with the 373 cases in the hospital during the year 1903. The duration of fever in the two former sets of cases proved precisely the same, 30.7 days; and exactly 8 per cent. of *relapses* occurred in these groups with 11 per cent. in the 1903 series. The average number of tub-baths (given every four hours if the temperature reached 102.5°) in the cases of urine flow below 100 ounces was 46; of those above 100 ounces, 38.6; of the 44 cases above 160 ounces, 32, pointing to greater remissions of temperature in the polyuria cases. *Bowel movements* were apparently little affected by the large amounts of water ingested, contrary to the expectation that constipation would be less common, and the proportion of cases with regular movements, constipation or diarrhoea was practically the same in the three contrasted series. *Retention of urine* occurred in the first twenty-four hours after admission in 2 cases, and in 1 was persistently troublesome. The thin, watery urine was well tolerated by the bladder, as a rule, and eighteen or twenty ounces were often passed at a time, though with a daily elimination of one or two gallons this involves frequent urination. As much less fluid was given at night, this does not imply disturbance of rest. There were 10 cases of *hemorrhage* in the polyuria group, 8 in the 56 cases below 160 ounces, and 2 in the 44 cases with more than 160 ounces, to compare with 12 per cent. and 6.7 per cent. of the other series. No one of these 10 hemorrhage cases was fatal. One case of *perforation* occurred in the 100 cases; 3 in the group of 50, and 15, the unusual percentage 4 in the 373 cases of 1903. *Phlebitis* was met with but once. The proportion in the other groups being 6 per cent. and 3.5 per cent.; and though the frequency with which venous thrombosis occurs

in typhoid varies much, it is conceivable that the copious water-drinking may lessen the tendency to the formation of agglutination thrombi. *Otitis media* was also infrequent, 3 cases developing, 3 per cent., with 3 in the 50 series, 6 per cent., and 16 in the 1903 series, 4.3 per cent.; and it seems plausible that the clean, moist mouths of these cases may well lessen the likelihood of middle-ear infection. *Meteorism*, however, usually of moderate but in some cases of considerable degree, was more common among the patients taking large quantities of water. Whether a coincidence or in any degree dependent on the treatment does not appear. The *skin* of these patients seemed less dry and harsh than usual; and *furunculosis* occurred only once or twice.

It is regretted that incompleteness of earlier records makes it impossible to compare with accuracy such symptoms as *headache*, *apathy*, *restlessness*, *insomnia*, and mild *delirium*; but the impression is strong in the minds of those who have cared for and watched these patients, whether nurses, house-staff, or the visiting physician, that just these toxic nervous symptoms of the disease, the symptoms so beneficially influenced by the cool-bath treatment of typhoid fever, are still more efficiently controlled by the copious water drinking, employed, of course, as an accessory, not a substitute means of hydrotherapy, and that patients are more comfortable for the treatment.

The total *mortality* of the polyuria group of 100 cases was five, 5 per cent. Four deaths occurred among the 54 cases with an elimination below 160 ounces, 1 death in the group of 46 cases where 160 ounces were exceeded. The latter case, after a severe illness, but when apparently convalescing satisfactorily, died on the sixth day of normal evening temperature, with an acute dilatation of the right heart. The other four fatalities were due, one to toxæmia one to perforation, one to laryngeal perichondritis, and one to peritonitis following an operation for suspected perforation. The mortality of the 308 cases in the hospital during the period under consideration from June, 1903, to October, 1904, and including the 100 polyuria cases, was 7.8 per cent., with twenty-four deaths. The mortality of the year 1903 was, however, usually large, 10.2 per cent. of a total of 373 cases, and the last half of this year with its large quota of patients not having such quantities of water internally, contributes two-thirds to the entire group of 308 cases. The death rate of the 105 patients discharged from the hospital during the eight months from January 1 to October 1, 1904, has been 6.6 per cent.

From March 1st to October 1st, the period during which all patients, with few exceptions, have received this form of treatment, there have been 77 cases with 3 deaths, 3.9 per cent, and, to date (October 11th) 86 cases with a mortality of 3.4 per cent. Finally, from April 1, 1904, to October 11, 1904, the rather unusual consecutive series of 56 cases without a death has occurred.

	Days of fever.	Highest temperature.	Number of baths.	Condition of bowels.				Complications.								Mortality.															
				Constipation.		Regular.		Diarrhoea.		Relapse.		Hemorrhage.		Perforation.		Otitis media.		Phlebitis.		Meteorism.		Total mortality.		Toxæmia.		Pneumonia.		Perforation.		Rare causes.	
				No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Below 100 ounces.	{ 50 cases.	30.7	104.5	46	38	23	46	4	8	4	8	6	12	3	6	3	6	3	6	7	14	6	12	1	2	2	4	3	0	0	
				23	43	20	36	10	18	5	9	8	14	1	2	2	4	0	0	14	25	4	7.2	1	2	0	0	1	2	2	4
Above 100 ounces. (Polyuria series).	{ Over 160 44 cases.	29.6	104.2	32	53	15	34	4	9	3	7	2	4	0	0	1	2	1	2	17	39	1	2	0	0	0	0	0	1	2	
				46	46	35	35	14	14	8	8	10	10	1	1	3	3	1	1	31	31	5	5	1	1	0	0	1	1	3	3
All cases, 1903.	{ 373 cases.	.....	.....	...	...	...	...	...	...	40	11	25	6.7	15	4	16	4.3	13	3.5	...	...	38	10.2	13	35	5	13	14	3.7	1.6	

As the 100 cases of typhoid fever with polyuria reported represent, in some measure, a selected group, the small and diminishing mortality rate is, of course, at the most, suggestive. It is felt, however, that certain conclusions as to the results and usefulness of this mode of treatment, which seems to supply an additional means of combating the toxæmia of the disease, may be submitted with some confidence with the hope that this method of copious water-drinking with its resulting diuresis, may be found by other observers to diminish in some further degree the severity and mortality of typhoid fever in hospital practice.

Our experience and conclusions may be summarized as follows:

1. Large quantities of water internally, a gallon or more in twenty-four hours, may easily be taken by typhoid fever patients, if administered in small quantities at frequent and definite intervals.

2. A copious elimination of watery urine at once follows, the degree of polyuria, day by day, closely corresponding to the quantity of fluid ingested.

3. Patients are more comfortable by this mode of treatment and toxic, nervous symptoms are lessened.

4. The mortality, as well as the severity, of typhoid fever, seems to be still further diminished by this method of hydrotherapy employed as an accessory to the cool-bath treatment of the disease.

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## CHLORIDE AND WATER EXCRETION IN TYPHOID FEVER, WITH COPIOUS DIURESIS.

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### I. INTRODUCTORY.

THE clinical tests of Drs. Cushing and Clarke, described in the preceding paper, offered an opportunity of investigating several interesting features of urine secretion in typhoid fever, as influenced by unusually large diuresis, the consequence of a very free administration of water. This opportunity we were glad to utilize as far as time would permit. To avoid complications, we confined ourselves to the study of the excretion of water and chlorine, neglecting all the other urinary constituents. The practical agreement of the results in all the cases examined shows that the material was sufficient to justify general conclusions.



We wish to take this opportunity to thank Dr. Cushing for the use of this clinical material, and the medical staff of Lakeside Hospital for their ready co-operation.

The details of the results are presented in the appendix, in the form of charts, and we shall confine ourselves to the discussion of the results. We shall touch but lightly on the bibliography of the subject, since this was discussed in the previous papers by Sollmann.<sup>1</sup>

While writing this paper, a monograph by Garratt<sup>2</sup> has come to hand which contains an excellent synopsis of the literature as well as valuable original contributions.

Concerning the cases included in this investigation, we may premise that they were all male subjects with typhoid fever of moderate degree, without fatality. All presented a trifling albuminuria. The study of each case was begun soon after admission to the hospital, and continued for a variable period, but never far into convalescence. The patients were confined to bed during the entire period of observation. For the greater part of the time they were on a milk and albumen diet;<sup>3</sup> during convalescence they received the diet noted in the appendix. All patients were given four ounces of distilled water every fifteen minutes. This as well as the food was omitted during sleep, and modified according to circumstances. This showed considerable irregularity.

All the patients excreted a very large quantity of urine of very pale color and of low specific gravity, containing an extremely low percentage of chloride.

## II. THE DIURESIS.

**THE DEGREE OF DIURESIS.** The quantity of urine excreted by these patients was very great. Excluding the period during which the administration of food was temporarily suspended on account

<sup>1</sup> American Journal of Physiology, 1902, vol. viii. p. 156; *ibid.*, 1903, vol. ix. p. 426.

<sup>2</sup> Medico-Chirurgical Transactions, 1904, vol. lxxxvii.

<sup>3</sup> The usual directions were that each patient should receive, every four hours, four ounces of milk with two ounces of lime-water, and every four hours alternating with the milk the white of one egg dissolved in six ounces of water, with a teaspoonful of sugar and a few drops of lemon-juice. A record of the feeding was directed to be kept. This showed considerable irregularity.

The analysis of these fluids yielded per litre:

### MILK AND LIME MIXTURE.

	Chlorides.	Nitrogen.
Sample I. . . . .	1.090	3.64
Sample II. . . . .	1.180	

### ALBUMEN-WATER.

Sample I. . . . .	0.445	0.14
Sample II. . . . .	.....	1.708
Sample III. . . . .	1.000	

of hemorrhage, the daily excretion of urine was generally above three litres, averaging over five litres, and exceeding nine litres on several isolated days.

The excretion of this enormous quantity of fluid is conclusive proof that the *kidneys are not appreciably injured* (at least under the conditions of these experiments) by typhoid fever or by prolonged diuresis. The conclusion is supported by the study of the urinary constituents, since the percentage of chlorides and the total molecular concentration depart very materially from those of the plasma. We will show later that the chlorides fall to extremely low figures, on some days below 0.1 gram per litre. The molecular concentration was only determined twice in the case of Kretzian. On July 16th the depression of freezing point was  $0.215^{\circ}$  C.; on July 19th,  $0.205^{\circ}$  C. This was probably the lowest point reached. It is pretty near to the recorded minimum ( $0.12^{\circ}$  C.).<sup>1</sup> The lowering of this factor below that of the blood ( $0.56^{\circ}$  C.) under the influence of water has been proposed as a test of renal efficiency. The present kidneys evidently bear the test very well.

The kidneys are also maintained very *efficient in the excretion of material*. The two cases of typhoid fever studied by Hatcher and Sollmann<sup>2</sup> are valuable for comparison, as the patients were kept under nearly identical conditions, except that only the usual quantities of fluid were administered, the urine measuring 650 c.c. to 1600 c.c. These cases showed a greater depression of freezing point ( $\Delta$ ) than the present series during the period of milk diet: Case N, mean  $\Delta$  equals 1.163; extremes, 0.859 to 1.446; Case B, mean  $\Delta$  equals 0.994; extremes, 0.991 to 0.997). On the other hand, the daily excretion of total molecules ( $\Delta \times$  c.c.) was much greater with the water treatment. With Kretzian,  $\Delta \times$  c.c. = 1935.0 on July 16th; 1758.9 on July 19th; whereas, in the cases of Hatcher and Sollmann,  $\Delta \times$  c.c. *never* exceeded 1428.5, the mean being about 900. We shall show later that the total excretion of chloride is also greater with diuresis than without.

Corresponding to the low molecular concentration, the *specific gravity* in the present series was also very low. Readings of the urinometer varied between  $-1.0$  and  $+2.8$ . No correction was made for temperature (summer heat), so that the real specific gravity is somewhat higher. In the case of Colson, the readings lay between 2 and 5 during polyuria, and between 9.8 and 12.5 when the quantity of urine was small (after hemorrhage).

DEPENDENCE OF THE DIURESIS ON THE INCOME OF FLUID.—The charts show that, with few exceptions, the curves for the income and output of fluid are strictly parallel, day by day. This is interesting as showing that the kidneys are capable of meeting efficiently even

<sup>1</sup> Fr. v. Koranyi. Berl. klin. Woch., 1899, Bd. xxxvi. p. 782.

<sup>2</sup> American Journal of Physiology, 1902, vol. viii. p. 139.

the not inconsiderable task imposed on them by the elimination of nine litres per day of urine of very low molecular concentration. For if the kidneys were at all unequal to the task, an accumulation of fluid would occur in the body, and the fluid would be excreted when the administration of water was discontinued, so that the urine excretion would exceed the fluid income whenever the latter was reduced. This does not occur at all, since the curves for ingestion of fluid and excretion of urine are so nearly parallel. Colson shows strikingly how the urine may fall in one day from 7000 c.c. to 3000 c.c., and Hickock from 5500 c.c. to 1300 c.c. by the reduction of the fluid. It is true that *intestinal hemorrhage* was present in both cases. If this had any effect it would favor retention of fluid; but the near approach of the output to income shows that this retention cannot be great.

The conclusion that no progressive retention of fluid occurs may also be seen by *comparing the income and outgo of water during longer periods*, as seen from the following table:

	Date of observation.	Days of observation	C.c. of fluid administered.	C.c. of urine collected.	Total deficiency in fluid excreted.	Deficiency in excreted fluid, average pr. day.
1. Colson, polyuria . . . .	July 11-19	9	48,720	33,540	15,180	1687
2. Colson, small urine . . . .	July 21-30	10	16,820	12,000	4,820	482
3. Hickock, polyuria . . . .	Aug. 15-17	3	18,840	15,600	3,240	1080
4. Hickock, small urine . . . .	Aug. 19-22	3	5,880	3,090	2,790	930
5. Kordick, polyuria . . . .	Aug. 19-Sept. 12	15	93,540	76,230	17,310	1154
6. Kretzian, " . . . .	July 12-30	19	157,020	155,300	1,720	90
7. Doyle, " . . . .	Aug. 15-17	3	17,560	17,610	-50	-17
8. Kiswan, incontinence of urine	Aug. 15-Sept. 2	19	120,780	94,470	<26,310	<1380
9. Barber, profuse sweating . .	Aug. 7-Sept. 2	6	48,540	18,840	29,700	4950

Excluding Cases 2, 4, 8, and 9, the average daily difference in the entire series equals 763 c.c., being but little larger than the average difference of Cases 2 and 4, with small urine secretion. In Case 6 the income and outgo practically balance; in Case 7, even more appears to be excreted than is administered. Cases 1 and 2 seem to show, indeed, that a greater amount of fluid is retained when the administration is large than when it is small, but the difference can probably be explained by differences in perspiration, due to the hemorrhages which occurred during the period of the lesser water administration.

We would also point out that the close agreement between the income and output of fluid shows that the elimination of the latter occurs to by far the greatest extent by the urine; only a relatively very small amount remains to be excreted by the bowels.

Accepting the conclusion that no appreciable progressive retention of fluid occurs after the administration of the water is well under way, it might still be supposed that a retention would occur during

the first days of administration, an equilibrium being established, somewhat as occurs in the administration of salt or bromides to normal individuals. Our charts do not answer the question directly, but the prompt and complete response of the urine curves to any change in the administration of the fluid, argues strongly against the initial retention. The chart also shows that the urine responds promptly and efficiently to the income of fluid, even after severe hemorrhage and withdrawal of fluid—*i. e.*, when the need of organism for water might be supposed to be the greatest.

**THE EFFECT OF PERSPIRATION ON THE DIURESIS.** This is seen very prettily in the case of Kordick. Free perspiration was noticed on the last two days of observation, and the chart shows a corresponding increase in the difference between the fluid and urine. Barber is perhaps a still more striking illustration. This patient had frequent chills, with sweating, between August 28th and September 2d. Accordingly the difference between fluid and urine averages 4950 c.c.—very much more than even the maximum average (1687 c.c.) observed in any of the other cases. Allowing 800 c.c. as the average apparent retention, Barber must have eliminated by the perspiration over 4000 c.c. per day more fluid than the other patients. This is very much more than the usual total loss by perspiration, as calculated by Garratt,<sup>1</sup> namely, 1200 c.c. for high fever, 1500 c.c. for high fever with remittance, 2068 c.c. in crisis, and 1096 c.c. in epicrosis.

This would indicate that the perspiration may be much more free with copious administration of water than it is ordinarily. This must be an important antipyretic measure. We would also emphasize that the quantity of urine was still very high (2500 c.c. to 4500 c.c.), notwithstanding the copious perspiration.

**THE EFFECT OF TEMPERATURE ON THE DIURESIS.** Since the administration of fluid was not kept perfectly constant, it would be difficult to determine the effect of the degree of fever, unless this effect were fairly large. The latter was certainly not the case, and it is our belief that the temperature has no great effect on the elimination of urine, except indirectly by influencing perspiration.

**THE EFFECT OF CATHARTICS ON THE DIURESIS.** These, by abstracting water through the bowels, should increase the difference between the income of fluid and the quantity of urine. This is shown by Kretzian, July 6th and 7th (see chart).

**EFFECT OF DIURETICS ON THE DIURESIS.** The charts show that the following diuretics certainly did not increase the quantity of urine: agurin, 6 grams per day; sodium acetate, 9 grams per day; potassium nitrate, 9 grams per day; urotropin, 2 grams per day. Indeed, the diuresis was generally less than in the control periods, the patients not being able to take as much water. This

<sup>1</sup> Loc. cit.

inefficiency of the diuretics during the existence of polyuria is an interesting phenomenon.

**CALCIUM CHLORIDE.** J. B. Macallum<sup>1</sup> has recently found that the injection of calcium chloride greatly diminishes the urine excretion in rabbits. Two of these patients, Hickock and Colson, received considerable amounts of this salt by mouth. It is somewhat difficult to judge the effects, as the administration coincided with the period of the water withdrawal; but comparing the hemorrhage period of Hickock, who received 4 grams of calcium chloride per day (August 17th to 22d) with the second hemorrhage of Colson, who did not receive calcium chloride (July 19th to 28th), no essential difference can be detected. It is, therefore, probable that the calcium does not influence the diuresis under these conditions.

### III. THE CHLORIDE EXCRETION.

The excretion of chlorides was low in these cases, both as concerns the quantity per day and per litre. Since a greatly lessened excretion of chloride is the rule in typhoid fever, it is necessary to compare the present series of polyuric patients with others in which the quantity of urine is no more than ordinary. The study published by Hatcher and Sollmann<sup>2</sup> is especially valuable in this respect, as the conditions other than water administration were practically identical in both series. We shall, however, avail ourselves also of other accessible data.

**THE EFFECT OF THE POLYURIA ON THE CHLORIDES.** This may be judged by comparing the averages of the two series of typhoid cases:

	Quantity of urine.	Chlorides per litre <sup>3</sup> (NaCl).	Chlorides per day (NaCl).
A. Polyuria (present series) <sup>4</sup> . . . . .	4500 c.c.	0.25 gm.	1.6 gm.
B. Ordinary quantity of urine (Hatcher and Sollmann) . . . . .	885	0.63	0.53
C. Various fevers above 100° (Garratt) . . . . .	958	0.90	0.88

The comparison of A and B shows that the polyuria, of about five times the normal, increased the elimination of chloride to about three times the normal, while it diminished their quantity per litre to about one-third.

This large polyuria, therefore, affects the chloride excretion in the same direction as it would in the normal kidney.

Lesser variations in the urine secretion also cause an inverse change

<sup>1</sup> Journal of Experimental Zoology, 1904, vol. i p. 179.

<sup>2</sup> American Journal of Physiology.

<sup>3</sup> The chlorides are always calculated as sodium chloride.

<sup>4</sup> Hickock and Colson are excluded, since they received calcium chloride, which might vitiate the conclusions.

in the concentration of the chlorides, but the daily elimination is scarcely affected. This may be seen from the following table:

	Mean quantity of urine (c.c.).	Mean chlorides per litre (gm.).	Mean chlorides per day (gm.).
Kretzian . . . . .	8000	0.17	1.5
Kordick . . . . .	5500	0.23	1.7
Kiswan . . . . .	4200	0.27	1.5
Barber . . . . .	4000	0.35	1.7

The study of the extremes also shows that the quantity per litre is more variable than the quantity per day.

	Minima.	Maxima.
Extremes of sodium chloride per litre . . .	0.09-0.20	0.27-0.60
Extremes of sodium chloride per day . . .	0.60-0.80	2.8 -3.2

The constancy in the limits of the daily chloride excretion is certainly very striking. It has been observed by other investigators.<sup>1</sup>

All these considerations, based on averages, justify the conclusion that *the degree of diuresis causes a parallel but small change in the total excretion of chlorides, and an inverse and considerable change in the percentage of this ion.*

It is difficult to verify these conclusions by the study of the individual curves. Indeed, at first glance it would seem that the percentage and daily elimination both varied in the same direction as the diuresis in the majority of cases. (For instance, Kordick, August 25th to September 2d; Kretzian, July 6th to 17th; Colson, July 19th to 28th; Kiswan, August 19th to 24th; Hickock, August 18th to 21st.) This, however, is a mere coincidence. A closer inspection of the curves shows that the percentage of the chlorides is really following the income of chlorides (which we shall study later), and that the latter is parallel to the income of fluid, and hence to the degree of diuresis. Indeed, the curve of the percentage of chlorides agrees better with the curve of the income of fluid than with that of the excretion of urine.

When there is a difference in diuresis independent of the admission of fluids—for instance, by perspiration, as in the case of Barber, and with Kordick on September 2d—the chloride obeys the general rule—*i. e.*, the daily quantity varies with, the percentage inversely to, the diuresis.

THE EFFECT OF PERSPIRATION ON THE CHLORIDES. Sweat contains about 0.3 per cent. of chloride, even in fever. It might be supposed, therefore, that the daily quantity of chloride and its percentage in the urine should both be lessened by profuse perspiration. The observations on Barber and Kordick do not bear this out. Evidently the excretion by the urine predominates so greatly over that by the sweat that the influence of the latter is totally obscured.

THE EFFECT OF THE FEBRILE CONDITION ON THE CHLORIDES. A careful comparison of the fever and chloride charts fails to reveal

<sup>1</sup> Garratt. Loc. cit., p. 21.

any correspondence. The chlorides usually drop to about 2 grams per day within three days of the inauguration of the milk diet, and tend to continue about this low point as long as the milk diet is continued, independently of the curve of the fever. They increase again when the patients are placed on convalescent diet, and often show very conspicuous oscillation at this time. The increase could, in most cases, be referred to greater chloride income (broth, etc.). This agrees with the general experience of most other investigators, in all febrile diseases except pneumonia. The only apparent effect of hemorrhage is seen in the simultaneous drop of the temperature and chlorides after hemorrhage (Colson and Barber). However, this is evidently due to the simultaneous stoppage of all food.

**THE EFFECT OF THE CHLORIDE INCOME ON THE CHLORIDE ELIMINATION.** Excluding the administration of calcium chloride (which will be considered separately), almost every change in the chloride income causes a corresponding change in the chloride elimination. There is apparently little tendency to retention. Even after severe hemorrhage and complete starvation, the chloride excretion responds promptly and completely to our increase of chloride income. It would be difficult to imagine a condition in which the need of the organism for chloride could be greater.

It is well known that the chloride excretion does not usually respond as promptly as this to changes in the chloride income, and that fever patients especially show a tendency to retention. We may perhaps suppose that the polyuria tends to reduce the chloride of the body to the extreme minimum, causing a ready elimination of any excess. It would seem to us that this is in fair agreement with Forster's theory,<sup>1</sup> although it could scarcely be cited as a proof of the latter.

We wished to determine also the effect of large additions of chlorides to the diet. The patient with whom we tried this (Colson) became nauseated, however, by the addition of 1 per cent. of sodium chloride to the water and milk, and absolutely refused to take the salt. In the face of this resistance we did not insist. The prompt and considerable rise in the chlorides in the convalescent period shows sufficiently that the elimination responds to large quantities of chlorides, but it does not permit any conclusions as to the completeness of the elimination.

**THE QUESTION OF CHLORIDE RETENTION IN FEVER.** We have seen that the degree of hyperpyrexia does not modify the chloride excretion in the present series of cases, and that this is the general result in all fevers, with or without polyuria. This does not, of course, imply that the disease process which underlies the hyperpyrexia has no effect on chloride excretion, independent of the hyperpyrexia. In the previous papers of Sollmann<sup>2</sup> the conclusion

<sup>1</sup> See T. Sollmann, *American Journal of Physiology*, 1902, vol. viii. p. 163.

<sup>2</sup> Loc. cit.

was drawn that "the disappearance of chloride from fever urines is due practically entirely to a deficiency of chloride income." This was based mainly on the observation that chloride excretion is influenced in the same direction as in health, arguing that the same mechanism is involved. While we see no reason to modify the latter conclusion, we believe that the phenomena are modified quantitatively in fever, in the direction of a much greater tendency to chloride retention. This may be seen from the following table of averages:

	Quantity of urine.	Sodium chloride per litre.	Sodium chloride per day.
A. Typhoid fever with polyuria . . . . .	4500 e.c.	0.25 gm.	1.6 gm.
B. Typhoid fever with ordinary quantity of urine . . . . .	885	0.68	0.53
Hatcher and Sollmann, Moos (quoted by Garratt)	.....	.....	0.9-3.4
C. Fevers above 100° (Garratt, loc. cit.) . . . .	958	0.90	0.88
D. Normal individuals on milk diet (Garratt, last day of No. 1, and second and third day of No. 2) . . . . .	965	2.75	2.7
Haskins <sup>1</sup> (fourth and fifth day). . . . .	1125	2.10	2.36

In fever, with milk diet (B and C) the daily excretion of chlorides by the urine averages between 0.53 to 0.88 gram,<sup>2</sup> and even with the large polyuria of the present series it averages only 1.6 grams, whereas in normal individuals on a similar diet it averages between 2.35 and 2.7 grams.

In this table the chloride income has not been considered, so that an absolute retention of chloride over the amount administered is not proven.

Haskins<sup>3</sup> gives data from which the absolute retention of chlorides may be calculated.<sup>4</sup>

From the first to the fifth day, inclusive, the chloride income was 14,508 grams; the excretion by the urine, 20,638 grams, a loss of 6.130 grams, or an average loss of 1.23 grams per day. Selecting the fourth and fifth days, when the conditions had reached a practical constant, the income was 7.25 grams, the output 4.71 grams, an average apparent retention of 1.27 grams per day. The loss by the feces and sweat must be subtracted from this. Röhmann determined the daily loss of chloride by the feces as 0.162 gram; there are no available data as to the loss by the sweat, but we see that even

<sup>1</sup> American Journal of Physiology, 1904, vol. x, p. 362.

<sup>2</sup> The higher figure of Moos may be excluded because it evidently does not refer to a milk diet.

<sup>3</sup> Loc. cit.

<sup>4</sup> In the tables given in Haskins' paper, the sodium chloride of milk is assumed to be 2.7 grams per litre, according to Bunge's figures. This seems to show a considerable chloride retention. There can be little doubt, however, that Bunge's figure is too high for the milk used by Haskins. Röhmann determined the chloride content of milk as 1.56 grams sodium chloride per litre; Schubert gives 1.6 grams; Soldner as 1.62 grams; Vanmeester as 1.74 grams; a sample analyzed by us gave 1.76 grams. We shall use 1.6 grams in the calculations.



in health a chloride retention of about 1 gram per day may occur with a chloride income of 3.63 grams per day. This agrees entirely with the figures of Javal, quoted by Garratt (page 37). While there can be little doubt, from the above table, that the retention in fever is greater than this by at least 1.5 grams per day, it is evident that the mere fact of retention is by no means characteristic of fever, and that the difference is merely quantitative and not qualitative.

On account of imperfect records and the variable chloride content of the albumin solution, we do not consider the data of the chloride income in the present series sufficiently exact to determine whether any chloride retention occurred. (In the case of Barber, assuming the albumin solution to contain 0.1 per cent. of sodium chloride, the chloride income was at least 7.282 grams for five days, the output, 5.125 grams, showing an average retention of at least 0.425 gram per day. In another case, however (Kiswan), the income in fourteen days was calculated as 20.603 grams, the output as 29.627 grams.) We are probably not far from right in assuming the average chloride income on a milk diet to be 2.4 grams of sodium chloride. On this assumption an ordinary typhoid patient retains 1.8 grams per day, the polyuria typhoid patient about 0.7 gram, and a normal individual about 1 gram. The conclusion seems justified that the polyuria is able to counteract the excessive chloride retention in fever.

**THE EFFECT OF CALCIUM CHLORIDE ON THE CHLORIDE EXCRETION.** We have shown that the chloride of the urine in this series of cases varies promptly with the chloride of the food. When the chloride is administered in the form of calcium chloride, the phenomena are altogether different. The charts show that in the case of Colson there was a latent period of six days, during which the administration of the calcium chloride did not increase the urinary chloride. A very considerable rise then occurred, especially in the percentage of chloride. It outlasted the stoppage of the calcium chloride by three days. In the case of Hickock there was no rise in the three days during which the urine was observed.

The total amount of chloride (calculated as sodium chloride) administered as calcium chloride to Colson between June 30th and July 9th equals about 31.05 grams.<sup>1</sup> To this must be added at least 10 grams for the food. During this time and in the four days following there were excreted at most 12.88 grams—*i. e.*, scarcely if any more than was given in the food. The calcium chloride has practically disappeared. Hickock shows a similar phenomenon.

It might be supposed that there was in these cases a real retention of chlorides, due to the hemorrhage. The prompt response of chloride excretion of added chloride in the diet inclines us against

<sup>1</sup> This is calculated on the assumption that the crystalline calcium chloride (containing six molecules of water) was given. We made no analysis of the sample, since small differences would not alter the conclusions.

this explanation. It seems more probable that the calcium hinders and delays the absorption of the chloride ion. Further observation would, of course, be required before accepting the latter explanation.

THE EFFECT OF OTHER SALTS ON THE EXCRETION OF CHLORIDES. The charts show that the following salts did not cause any change beyond the normal accidental variations in the quantity of urine or in the chlorides per litre or per day: agurin, 6 grams per day (one trial of two days); sodium acetate, 9 grams per day (four trials of three days, one trial of two days); sodium nitrate, 9 grams per day (five trials of three days, one trial of four days). This negative result, as concerns the chlorides, does not seem to be due to absence of diuretic effect, for Garratt obtained a similar negative result on the chlorides, in various fevers, with caffeine, digitalis, potassium citrate, sodium bicarbonate, citrate, and salicylate. In normal individuals on a milk diet (Haskins) diuretin and sodium acetate also did not modify the chloride excretion, although the acetate had a considerable diuretic effect.

We intended to make further experiments with *iodides*, but could not find the time; an experiment was, however, made by accident in the case of Barber. On September 1st the urine contained 0.345 gram of chloride per litre, and 0.95 gram per day, and it averaged about this for the preceding four days. On September 2d the urine after incineration titrated 1.945 grams per litre, and contained iodine. On extracting the latter it was found to correspond to 1.714 grams of sodium iodide, leaving 1.280 grams of sodium chloride per litre or 2.419 grams of chloride per day. It is seen that the accidental administration of the iodide increased the percentage of chloride 3.7 times, the daily excretion 2.6 times—a very conspicuous difference.

In a previous research Sollmann<sup>1</sup> had observed that in dogs, when the urine had been rendered chloride poor by the injection of sodium sulphate, the percentage of chloride was increased by the intravenous injection of sodium iodide and sulphocyanide, but was not increased by diuresis, caffeine, or irritant diuretics, nor by the intravenous injection of the acetate, ferrocyanide, or phosphate of sodium, nor by the injection of urea, alcohol, or glucose. Several investigators had shown, on the other hand, that in rabbits these diuretic measures increase the percentage of chloride (except the administration of water by mouth). This seems to show an important difference in the chloride retaining mechanism in these two classes of animals, and it seems interesting to determine to which class the human kidney belongs. This was the primary object of the present research. The negative effect of the acetate, agurin, and urotropin seems to indicate that the chloride excretion in man resembles that in the dog. This was also the conclusion of

<sup>1</sup> American Journal of Physiology, 1903, vol. ix. p. 426.

Haskins. It must be remembered, however, that the doses of the salts are much smaller than those which were used on the dogs, and we cannot be certain that correspondingly large doses would not have increased the percentage of chlorides. The positive result with the iodide shows, however, that even moderate doses of this salt, which is effective on dogs, are also effective in man. On the other hand, sodium nitrate, which is very effective in dogs, produced no certain effect in man. This may, however, be due to the rapid destruction of the nitrate ion in the body.

We may conclude, further, that a moderate *nephritis* does not break down the chloride retaining mechanism, since all the cases had albuminuria. This is also the conclusion of other investigators.

#### SUMMARY AND CONCLUSIONS.

The free administration of water to typhoid patients causes a large polyuria, exceeding three litres per day and averaging over five litres. On isolated days nine litres are not rarely excreted. The percentage of chlorides and the total molecular concentration are much below normal, while the daily excretion of total dissolved molecules exceeds that of ordinary typhoid cases. The eliminating capacity of the kidneys is, therefore, not injured in typhoid fever, nor by a prolonged polyuria. No accumulation of fluid appears to occur in the body, the excretion being very nearly parallel to the income. The quantity of urine is influenced by the perspiration and to a lesser extent by catharsis. It appears probable that the perspiration is freer under the influence of the large administration of fluid. The temperature has no direct effect on the diuresis. Diuretics do not increase the polyuria, nor does the administration of calcium chloride appear to diminish diuresis.

The effect of the polyuria on the chloride excretion, as compared with ordinary typhoid cases, consists in a diminution of the percentage and an increase of the amount excreted per day. Minor variations in diuresis effect the percentage, but not the daily output. Perspiration acts indirectly, by influencing the diuresis. The course of the fever, the degree of hyperpyrexia, and the convalescence appear to have no direct effect.

The chloride excretion varies strictly with the chloride income. The effect of calcium chloride is, however, delayed and comparatively small. Agurin, sodium acetate and nitrate, and urotropin had no effect on the chloride excretion, but it was increased by iodide. Moderate nephritis was without effect.

The excretion of water and chlorides in typhoid fever appears to obey the same laws as in health. There is, however, a greater tendency to chloride retention in the fever. The difference appears to be only quantitative and not qualitative. It is greatly diminished by polyuria.

The prolonged restriction of the chloride income appears to produce no deleterious effects, and the patients do not develop any "salt hunger."

#### APPENDIX.

**EXPLANATORY NOTES.** The urines were collected from 7 A.M. to 7 A.M., the last collection being made very close to 7 o'clock. The urines were analyzed soon after their receipt at the laboratory. The *chlorides* were determined in a 20 c.c. sample of the urine, directly by titration against silver nitrate (1 c.c. = 1 mg. NaCl), using potassium chromate as indicator. This preliminary determination served to show the progress of the case, and to check the second determination. This was made after incinerating 20 c.c. of the urine with sodium nitrate and carbonate. The latter determination was used in calculating the daily excretion. The direct determination gave results but slightly higher than the incinerated samples during the polyuria, when the urine was almost colorless. In the scanty, highly colored urines which were voided after the hemorrhages the end reaction was indistinct and the values were considerably too high.

The recording of the fluid taken and the collection of the urines had to be left to the nurses and orderlies. As this conflicted somewhat with numerous other duties, occasional errors were only natural. When these were discovered the results were discarded, which accounts for some of the breaks in our charts. There can be little doubt that other errors escaped detection, which may account for temporary, unexplained variations. These we have retained in the charts, but we have tried to eliminate them in drawing our conclusions. A fairly good check of the accuracy of the collection and recording is furnished by comparing the curves for the income of fluid and the quantity of urine, and the income and output of chlorides. From these we may conclude that the accuracy was sufficient.

The figures for the chloride income cannot be considered absolute, and have only a comparative value. In their calculation the first analysis of the albumen solution (0.445 gram per litre) and of the milk (1.09 grams) was employed.

#### SUPPLEMENTARY NOTES.

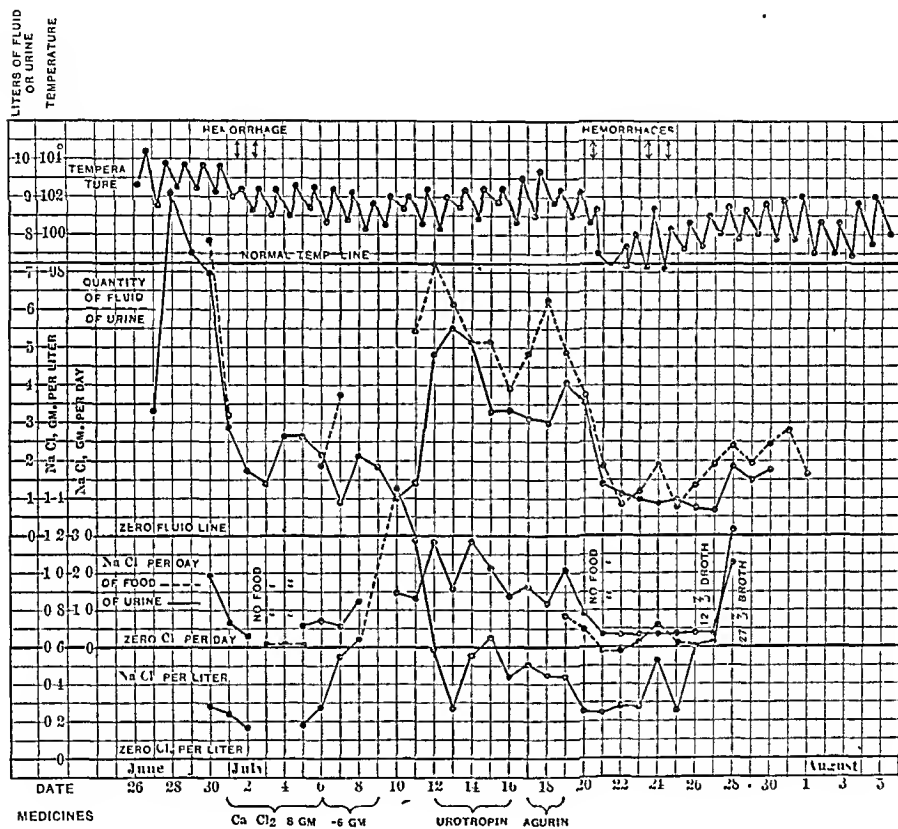
(Mention of medicines like strychnine or morphine and the tub-baths are omitted.)

**COLSON.** Admitted to the hospital and placed on milk and albumen diet and water on June 26, 1904, on the eighteenth day of the disease. The urine shows a faint trace of proteid throughout.

*Diet.* Milk and albumen-water to July 2d; July 2d to 5th, all nourishment stopped and water reduced; July 5th to 15th, milk and

albumen-water; July 15th, soft egg and toast; July 16th to 20th, custard and junket (July 18th, 3 ounces of ice-cream); July 20th to 22d, all nourishment stopped and water reduced; July 22d, albumen-water; July 23d, milk and albumen-water; July 24th, albumen-water; July 25th, milk and albumen water; July 26th, milk, albumen, custard, and 13 ounces of broth; July 27th, custard, junket, and 27 ounces of broth. (Port wine from July 24th on.)

CHART I.—COLSON.



*Medicines* (per day). July 1st to 6th, 8 grams calcium chloride; July 6th to 9th, 6 grams; July 12th to 16th, 2 grams urotropin; July 17th to 19th, 6 grams of agurin.

*Intestinal Hemorrhages.* July 2d, 5 A.M., 3 ounces; 9 A.M., 6 ounces; 3 P.M., 16 ounces; July 20th, 3 P.M., four hemorrhages, aggregating 52 ounces; July 24th, 1 A.M., 12 ounces; 3 P.M., 4 ounces.

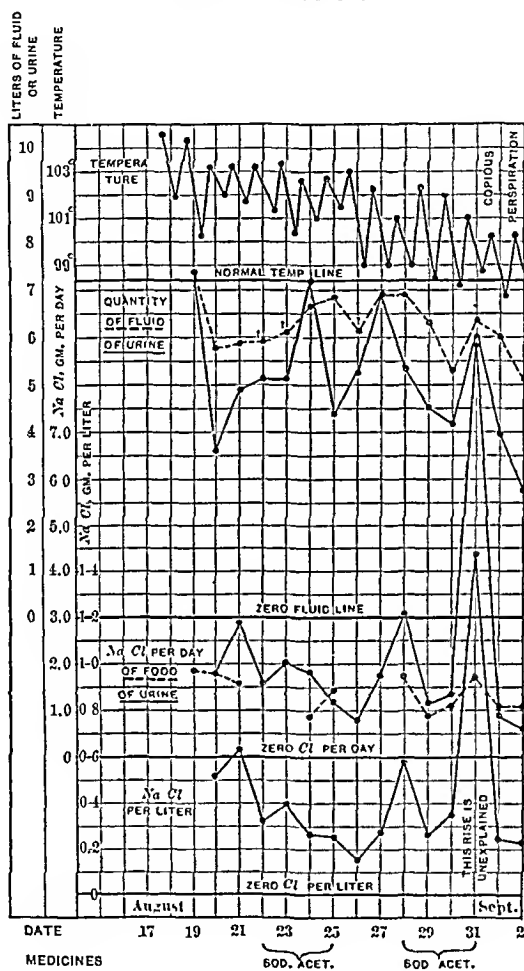
**KORDICK.** Admitted to the hospital and placed on milk and albumen diet and water on August 17th, on the fourth day of the disease. Faintest trace of albumin throughout. Perspires freely, especially on August 31st and September 1st.

*Diet.* Milk and albumen-water.

*Medicines* (per day). August 22d to 25th and August 28th to 31st, 9 grams of sodium acetate.

KRETZIAN. Admitted to the hospital and placed on milk and albumen diet and water on June 28th, on the fourth day of the disease. Slight albuminuria throughout.

CHART II.—KORDICK.



*Diet.* To July 28th milk and albumen-water (July 17th, bag of candy found in bed; not known whether any was eaten; no visitors allowed after this); July 18th, 3 ounces of ice-cream; July 22d, 4 ounces of ice-cream; July 28th, custard and junket; July 29th, toast and egg.

*Medicines* (per day). July 4th to 6th, 9 grams of sodium acetate; July 6th to 10th, 17th to 20th, and 24th to 27th, 9 grams of sodium nitrate; July 6th, 0.2 gram of calomel; July 7th, 15 grams of magnesium sulphate.

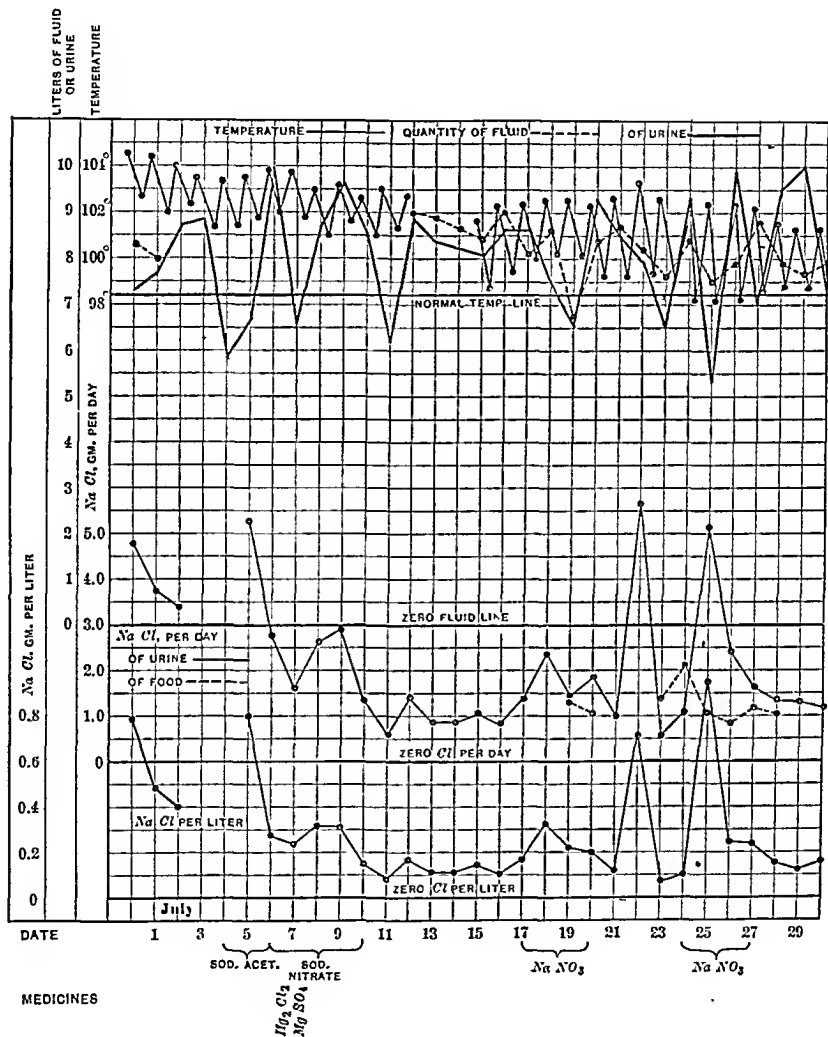
KISWAN. Admitted to hospital and placed on milk and albumen diet and water on August 6th, on the eleventh day of the disease.

An active nephritis exists on admission, which tapers off. Some urine is lost through incontinence.

*Diet.* Milk and albumen-water throughout.

*Medicines* (per day). August 18th to September 2d, 0.67 gram of urotropin; July 18th to 19th, 6 grams of sodium nitrate; July

CHART III.—KRETZIAN.



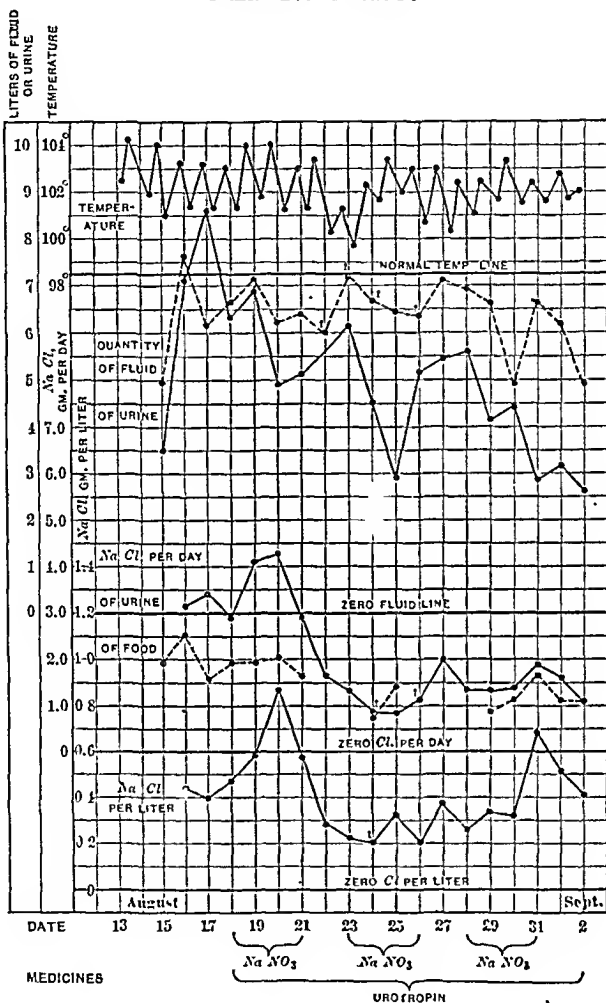
19th to 21st, 23d to 26th, and 28th to 31st, 9 grams of sodium nitrate.

**HICKOCK.** Admitted to hospital and placed on milk and albumen diet and water on August 8th, the eleventh day of the disease. A very faint trace of albumin throughout.

*Diet.* Milk and albumen-water, except from August 18th to 20th, when all nourishment is withdrawn and the water reduced.

*Medicines* (per day). August 17th on, 4 grams of calcium chloride; August 18th, 6 grams of sodium acetate; August 19th to 21st, 9 grams of sodium acetate.

CHART IV.—KISWAN.



*Intestinal Hemorrhages.* August 17th, 9 to 12 A.M., 6 ounces; August 18th, 5 to 9 A.M., 3 ounces; 3 to 6 P.M., 4 ounces; August 20th, 6 to 9 P.M., 10 ounces.

**BARBER.** Admitted to hospital and placed on milk and albumen diet and water on August 19th, the sixth day of the disease. The urine contained a faint trace of albumin throughout.

*Diet.* Milk and albumen-water.

*Medicines* (per day). August 27th to 30th, 9 grams of sodium acetate; August 30th, 0.67 gram of quinine hydrochloride; August 31st to September 2d, 1 gram. Iodide was found in the urine on September 2d.



CHART V.—HICKOCK

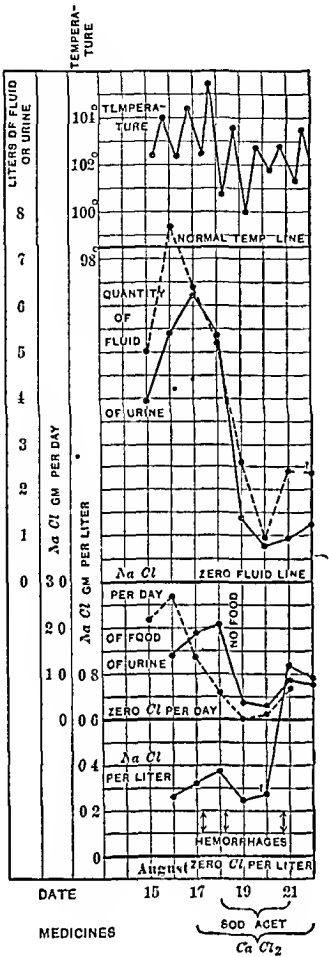
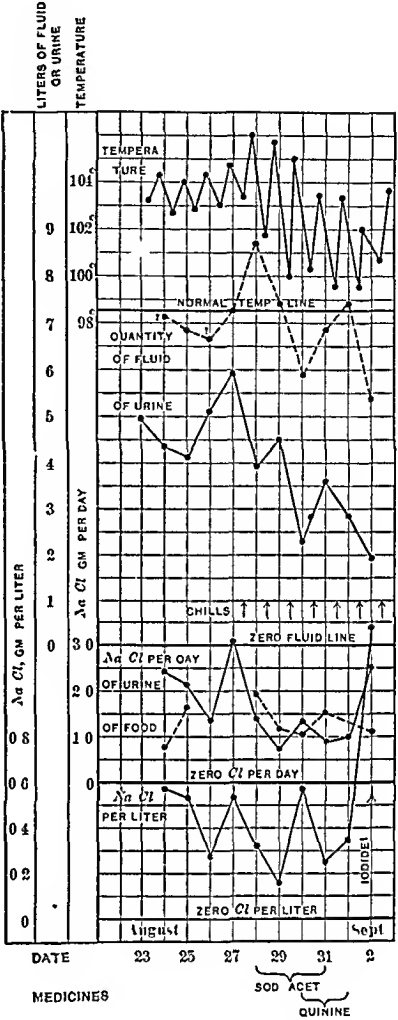


CHART VI.—BARBER



*Chills*, accompanied by profuse perspiration, were present from August 7th.

DOYLE. Admitted to hospital and placed on milk and albumen diet and water on August 11th, the fourteenth day of the disease.

# STUDIES ON THE BASOPHILIC GRANULATIONS OF THE ERYTHROCYTE IN LEAD POISONING AND OTHER CONDITIONS, WITH SPECIAL REFERENCE TO THE RELATION WHICH THEY BEAR TO THE NUCLEI OF THE RED BLOOD CORPUSCLES.

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THE etiology and significance of basophilic granulations occurring in the erythrocytes of the circulating blood of man have been much discussed in recent years and variously interpreted. These granulations were seen by many of the earlier writers in the erythrocytes of individuals presenting various forms of anæmia. By some, they were thought to represent the remains of a pre-existing nucleus, and their presence seemed to indicate the means whereby the normoblast lost its nucleus and became an adult red corpuscle.

Grawitz<sup>1</sup> found basophilic granules in cases of pernicious anæmia, not only in the erythrocytes, but also in the nucleated red blood corpuscles. The erythrocytes containing these granules he noticed increased in numbers as the anæmia became more severe, and decreased with improvement. They were, however, entirely absent in the bone-marrow of severe cases. He also found them present in the blood of more than thirty cases of lead poisoning, their numbers being in direct proportion to the severity of the symptoms, while in some cases they were the only sign of lead poisoning. The fact that granules were frequently found in the protoplasm of nucleated cells, the nucleus of which was apparently normal, he thought was evidence that the granules were not the product of nuclear fragmentation.

As a result of his studies Grawitz concluded that these granules are due to a degenerative process affecting the hæmoglobin of the red corpuscles, a condition which is produced by the action of some definite blood poison.

White, Pepper,<sup>2</sup> and Stengel<sup>3</sup> examined the blood of twenty-one lead workers without subjective symptoms, and found basophilic granules in the red corpuscles of every case. In five of their cases they found small numbers of nucleated red corpuscles in each slide, but they do not speak of having made a total count of the erythrocytes. They were able to demonstrate the granules in red corpuscles of dogs after administering small doses of lead acetate

<sup>1</sup> AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1900, vol. cxx. p. 278

<sup>2</sup> *Ibid.*, 1901, vol. cxxii. p. 266.

<sup>3</sup> *Ibid.*, 1902, vol. cxxiii. p. 673.

by mouth, and found that in all their experimental cases the earlier granules showed a greater tendency to clump and cling together than did the later. They also state that in their experiments upon dogs it was a very common observation to find nucleated red corpuscles associated with the granular cells.

Simon<sup>1</sup> studied the blood of twenty cases of lead poisoning and found basophilic granules constantly present in the red blood corpuscles. He was also able to demonstrate granules in the red blood cells of two of his fellow-workers seventy-two hours after the administration of six grains of lead acetate by mouth. In one of these experiments the lead acetate was continued until abdominal pain and constipation were produced. The lead was then stopped and many granular cells were found in the blood. Six days after this one normoblast was found in one slide studied, but this individual he states was somewhat anæmic, as indicated by a slight reduction of the hæmoglobin percentage. He makes no mention of a total count of the red blood corpuscles per 1 c.mm. White, Pepper, Stengel, and Simon all seem to agree with Grawitz as to the origin and significance of these granulations.

Schmidt<sup>2</sup> performed a series of interesting experiments upon animals poisoned by lead salts and phenol-hydrazine, by which means he was able to demonstrate the presence of many granular cells as well as nucleated red corpuscles in the peripheral circulation. He states that there was no essential difference between lead poisoning and phenol-hydrazine poisoning in his experimental cases. Further, he injected a rabbit intraperitoneally with a solution of phenol-hydrazine and shortly after inoculation examined the blood from different parts of the body, including the ear. In every specimen many granular red corpuscles and many nucleated red cells were seen. From this experiment it was evident that the changes brought about by this drug affected the red cells of the whole circulation. He then repeated the same experiment, but before the drug was injected one ear was ligated. The blood was studied as before, being taken from various parts of the body as well as from the ligated ear. Specimens obtained from the body showed many granular red corpuscles and nucleated red cells, but in preparations made from the ligated ear granular cells were entirely absent, and nothing but normal blood elements were seen. In many of his experimental cases Schmidt found nucleated red cells the nucleus of which appeared to be undergoing various forms of dissolution; not only were they found in the peripheral circulation, but in the bone-marrow as well. He came to the conclusion that these basic-staining granules were the remnants of a broken nucleus, and that the process had its origin in the blood-forming organs and not in the general circulation.

<sup>1</sup> International Clinics, 1902, vol. i. p. 69.

<sup>2</sup> Exp. Beitr. z. Path. d. Blutes, Jenna, 1902.

Vaughan<sup>1</sup> studied the blood from normal individuals and from cases of both primary and secondary anæmias. He could demonstrate basic-staining granules in the erythrocytes of healthy persons and concluded that they were normally present in small numbers. Under certain pathological conditions they were increased, but no very great elevation was noted, excepting in blood containing many nucleated red corpuscles. He came to the conclusion that these granules were undoubtedly the product of a nucleus that had undergone dissolution.

In the routine examinations at the Pennsylvania Hospital of the blood of individuals poisoned by lead, nucleated red corpuscles were found so frequently in association with the granular cells, even when the total number of red corpuscles was only very slightly reduced, that it was thought there might be some relation between these two varieties of cells. The following study of the blood was undertaken with the object in view of determining if possible what this relation, if any, might be:

1. Blood of apparently normal individuals.
2. Eleven lead workers without subjective symptoms.
3. Sixteen cases of lead poisoning in the wards of the Pennsylvania Hospital.
4. Various forms of primary and secondary anæmias in the wards of the Pennsylvania Hospital.

The following examinations were made in each case:

1. Estimation of percentage of hæmoglobin.
2. Estimation of total number of erythrocytes per 1 cm.
3. Estimation of total number of leukocytes per 1 cm.
4. Differential count of 500 leukocytes and estimation of number of nucleated red corpuscles.
5. Estimation of percentage of red corpuscles containing basophilic granulations.

The hæmoglobin was estimated by Dare's hæmoglobinometer and the erythrocytes and leukocytes counted by means of the Thoma-Zeiss instrument. The differential leukocyte count was made after preparing smears on clean glass slides in the usual manner, and staining them with Wright's modification of Leishman's stain. In studying the basophilic granules Jenner's, Theonin-pheniqué, and Wright's stains were all tried, but none of them proved nearly as satisfactory as the method of using polychrome methylene blue recommended by Vaughan. This technique was therefore used in each case. The method as described by him is as follows:

"The ear of the patient whose blood we wish to examine is thoroughly cleansed of all dirt particles, by washing with alcohol. The blood is then drawn, the first drop being used as an index as to whether a free flow has been obtained or not. This is then

<sup>1</sup> Journal of Medical Research, vol. x. p. 342

wiped off with a clean towel and a drop of the previously filtered stain is placed over the site of puncture by means of a clean glass rod or pipette. The blood flowing from the wound then mixes directly with the stain without coming in contact with the air, and the small drop thus obtained is immediately collected on a cover-slip and placed at once upon a clean slide, where, if the drop is not too large and the slide and cover are clean, it spreads out into a thin film and may be examined at once." The stain used was Unna's polychrome methylene blue as prepared by Grüber.

In estimating the number of red cells containing granules with this method of staining a one-twelfth oil-immersion lens was used. One thousand red corpuscles were counted and the percentage of granular cells to non-granular cells calculated. It cannot be said that this is an absolutely accurate method, but after a little practice in staining the results will be quite uniform and only vary very slightly; in many instances not at all. This is by far the best method of studying the granules, as they can be very easily demonstrated when they exist in small numbers. It is the only method that I know of by which the granules can be found in normal blood. The blood of five apparently normal individuals was examined, and in each specimen red corpuscles containing basic-staining granules were present. Their number varied, in the different specimens examined, from 0.4 of 1 per cent. to 1.6 per cent. in 1000 red corpuscles counted. The hæmoglobin percentage and total number of red and white corpuscles were normal, while the red corpuscles containing granules, as well as those without granules, presented no abnormal changes. With Wright's stain granules could not be found in the red corpuscles.

TABLE I.—Lead Workers without Symptoms.

	Per ct. of hæmoglobin.	Red cells per 1 c.mm.	Per ct. of granular red cells.	Number of nucleated red cells found while counting 500 leukocytes	Remarks.
1	75	4,264,000	3.4	0	Exposure slight; never had symptoms.
2	70	3,400,000	2.8	3	" continuous and moderate for 18 years.
3	85	4,732,000	0.8	0	" very slight; never had symptoms.
4	80	3,256,000	9.6	1	" great; had one attack of colic.
5	70	4,116,000	5.6	1	" moderate; had one attack of colic.
6	70	4,300,000	5.3	1	" " " " " "
7	90	4,040,000	3.7	0	" slight; never had symptoms.
8	70	3,404,000	4.0	1	" great; never had symptoms.
9	75	4,560,000	6.5	0	" great; marked tremor of hands.
10	90	3,800,000	3.6	1	" great; had one attack of colic.
11	90	4,868,000	1.3	0	" slight; never had symptoms.

Table I. shows the results of the examinations of the blood of eleven lead workers without subjective symptoms. All these examinations were made in the factory where the men were actually engaged at their various duties. The exposure varied somewhat in degree, but the men were all more or less exposed to lead dust while at work. On examining this table it will be seen at once that there was only a slight reduction of both the hæmoglobin and the total number of red corpuscles, and that they were reduced in the same relative proportions. Seven cases had a total red count of more than 4,000,000, the two highest of which is No. 3 and No. 11, while only four were below 4,000,000, the lowest being No. 4. All but two show a decided increase in the number of granular red corpuscles, while five cases presented one nucleated cell in the smear, and one presented three nucleated red cells. These cases certainly show a very mild type of anæmia, but still six of them had nucleated red corpuscles in their peripheral circulation.

TABLE II.—Sixteen Cases of Lead Poisoning in the Wards of the Pennsylvania Hospital.

	Per cent. of hæmoglobin.	Red cells per c.mm.	Leukocytes per c.mm.	Per cent. of red cells showing basophilic granules counting 1000 reds.	Number of normo- blasts seen while counting 500 leuko- cytes.	Number of megaloblasts seen while counting 500 leuko- cytes.	Poikilocytosis.
1	72	2,828,000	7,500	18.0	4	0	Marked.
2	67	4,852,000	7,200	.....	2	0	Moderate.
3	80	4,028,000	10,200	.....	5	0	"
4	88	4,785,000	12,200	.....	4	0	Slight.
5	76	4,400,000	8,500	.....	2	0	"
6	98	4,680,000	7,300	.....	2	0	Moderate.
7	70	2,620,000	6,200	5.0	2	0	Marked.
8	85	4,424,000	5,800	6.3	2	0	Slight.
9	78	4,472,000	12,550	13.0	3	0	"
10	82	4,672,000	9,450	9.5	1	0	"
11	76	3,800,000	7,000	14.0	130	13	Moderate.
12	76	3,860,000	7,500	9.2	75	9	"
13	76	3,850,000	7,400	18.0	10	0	"
14	82	4,056,000	5,800	.....	2	0	Slight.
15	68	3,356,000	11,750	14.4	25	4	"
16	65	2,976,000	7,600	7.8	2	0	"

In Cases 2, 3, 4, 5, 6 and 14 granular cells were increased, but percentage not estimated.

Table II. gives the results of the blood examinations of sixteen cases of lead poisoning from the wards of the Pennsylvania Hospital.

All these cases presented the typical picture of poisoning: colic, constipation, blue line on gums, tremors of extremities, etc. One patient had wrist-drop. The symptoms were well defined in all cases, though in some they were more severe than in others. The hæmoglobin and number of red corpuscles were not reduced much more than in the previous series of cases. The red corpuscles in only three instances were below 3,000,000, although there were the most evident signs of poisoning.

TABLE III.—Ten Cases of Anæmia Including both Primary and Secondary Varieties.

	Per ct. of hæmoglobin.	Red cells per c.mm.	Leuko-cytes per c.mm.	Per ct. of red cells showing granulations in 1000 reds counted.	Number of normoblasts seen while counting 500 leukocytes.	Number of megaloblasts seen while counting 500 leukocytes.	Diagnosis.
1	22	980,000	5,600	0.2	2	0	Hodgkin's disease.
2	72	2,968,000	6,600	3.9	0	0	Carcinoma of stomach.
3	40	2,576,000	5,800	1.9	0	0	Fibroma of uterus.
4 Mar. 14	85	4,390,000	12,000	2.0	0	0	Phenacetin poisoning.
4 Mar. 16	80	3,728,000	11,000	2.8	0	0	Phenacetin poisoning.
4 Mar. 17	73	3,492,000	10,800	0.8	0	0	Phenacetin poisoning.
5	80	4,572,000	4,400	1.5	0	0	Carcinoma of liver.
6	50	2,380,000	9,000	2.3	0	0	Hypertrophic cirrhosis of liver.
7	60	2,984,000	.....	3.9	0	0	Typhoid relapse.
8 May 5	30	1,824,000	6,900	10.3	2	0	" "
8 May 16	26	1,216,000	5,400	5.0	0	0	" "
8 May 16	27	1,328,000	5,900	5.2	0	0	" "
9 May 24	48	1,432,000	5,000	9.8	1 (250 leuk. counted)	0	Pernicious anæmia.
10	35	1,148,000	3,200	17.0	9 (250 leuk. counted)	6	Banti's disease.

The number of granular cells was decidedly increased in every case. There was, moreover, a much greater increase than in slides from lead workers presenting no subjective symptoms. This would naturally be expected. (In six of the cases the percentage of granular cells was not estimated, but it may be said that they were markedly increased in numbers.) Accompanying this increase of granular cells there was in each case one or more nucleated red corpuscles. In Nos. 11, 12, 13 and 15 enormous numbers of nucleated red corpuscles were found, some of them being typical megaloblasts.

In all of these cases of anæmia (Table III.) red corpuscles with granulations were invariably found and were increased slightly, while if the blood contained nucleated red corpuscles the increase was very marked.

The granules contained in the red corpuscles, in all the cases observed here, may be divided into three general classes, based upon their morphological appearance and their affinity for nuclear stains. These three groups I will call Nos. 1, 2 and 3.

1. Fine and coarse thread-like strands.

2. Fine dot-like granulations.

3. Dense coarse mass.

1. In the normal blood, when stained as previously described with polychrome methylene blue, a few red corpuscles were seen containing fine dot-like granules connected by delicate thread-like strands running irregularly through the cell. These strands varied in numbers and in length. Sometimes only one strand was seen in a cell extending through a quarter or the whole of its diameter, while other cells presented two or three such delicate threads often overlapping one another and suggesting in appearance a network. In color, they varied from a light lilac through all the intermediate shades to a dark blue. This type of granulation was seen in the blood of every case that was studied, whether normal or pathological, and was the predominating type present in the blood of primary and secondary anæmias, as well as of the more severe cases, due to lead poisoning. (See Plate, Fig. I., a.)

When the normal blood was stained by any other method these granulations could not be demonstrated.

2. The second variety of granulation was found in greatest numbers and most constantly in the blood of lead workers without symptoms, although constantly present in all the lead-poisoning cases studied and occasionally found in the primary anæmias.

These granulations varied from very minute, pinpoint-like granules to the size of an eosinophile granule, irregularly scattered throughout a red corpuscle, varying in color from a light blue to almost black. Sometimes there would only be four or five of these granules in a cell, but frequently they were so numerous that it was impossible to count them. The red corpuscles containing this type of granulation were of all varieties: microcytes, macrocytes, poikilocytes, polychromatophilic cells, and a few nucleated red corpuscles.

With Wright's stain they were easily and constantly found in all cases of lead poisoning and in a few of the primary anæmia cases. (See Plate, Figs. I., II., b, III.)

3. The third type was found in many instances of lead poisoning, but this particular form of granulation was perhaps more numerous than the other varieties in those cases of lead poisoning where



nucleated red corpuscles were plentiful. (See Cases Nos. 11, 12, 13 and 15, Table II.)

The red cells containing these granulations were, as a rule, normal in appearance, while others were smaller or larger than normal. There was never any change in shape.

The granules consisted of a dark-blue staining mass about the size of the nucleus of a normoblast. This mass was generally placed in the centre of the red cell, appeared distinctly granular, and was slightly ragged in outline. Occasionally one or two small blue granules, entirely separated from the central mass, were noticed near the periphery of the cell. (See Plate, Fig. I., c.)

I am convinced that these three varieties of granulations represent different stages in the dissolution of the nucleus of the red cell.

When Wright's stain was used many of the nucleated red corpuscles observed in smears taken from cases of lead poisoning presented small, blue-staining granules, scattered through their protoplasm. The color of these granules in every instance was the same as that of the nucleus. In a few instances the nucleus of the normoblasts stained poorly; its outline was somewhat indistinct, slightly ragged, and decidedly granular, suggesting that particles had been broken off from its edge. (See Plate, Fig. II., d.)

Many apparently normal red corpuscles containing a small, round, pale-blue, granular mass were noticed. Such cells might easily be interpreted as normoblasts, the nuclei of which had undergone some degenerative process. It was very difficult to distinguish these structures from platelets resting upon a normal red corpuscle, so that I am unprepared to diagnose this cell.

In one case of pernicious anæmia many megaloblasts were present, the nuclei of which were certainly breaking up, and many blue-staining granules were scattered throughout the protoplasm of the cell.

It is generally conceded by most observers that the presence of normoblasts and megaloblasts in the circulating blood is an indication of a regenerative process on the part of the blood-forming tissues, and by some the appearance of macrocytes and microcytes is interpreted in the same way.

In general, it may be said that nucleated red corpuscles are not present in the circulating blood unless there is a reduction of at least 50 per cent. of the total number of red corpuscles, and even then they occur only in small numbers.

Anæmia has always been spoken of as one of the characteristic signs of lead poisoning, but the exact degree of anæmia has very seldom been mentioned.

Red corpuscles containing basic granulations have frequently been found in the blood of experimental cases, and, as in Schmidt's experiments, nucleated red cells have occasionally been found. When the latter cells were present they were thought to indicate an acute and severe type of anæmia.

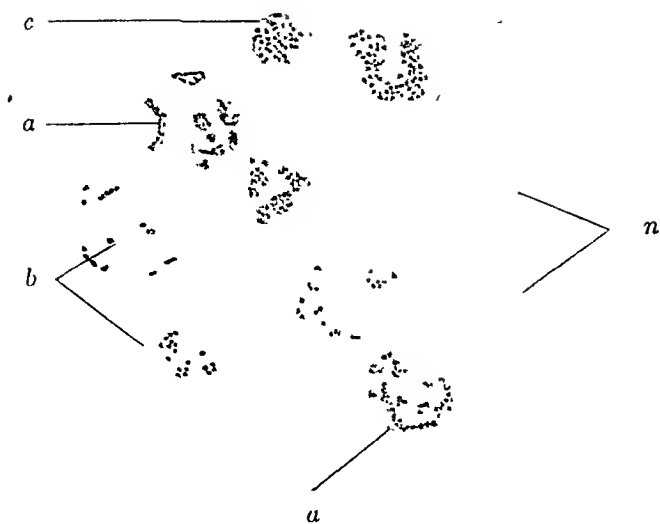


FIG. I.



FIG. II.

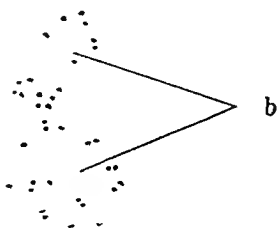


FIG. III.

FIG. I.—Red blood corpuscles from case of lead poisoning, stained with polychrome methylene blue, showing three types of granulations, *a*, *b* and *c*; also normal red cells, *n*.

FIG. II.—Red blood corpuscles from case of lead poisoning, stained with Wright's stain, showing granulations, type *b*, and normoblast, *d*.

FIG. III.—Red blood corpuscles from case of lead poisoning, showing granulations, type *b*, stained with saturated solution of methyl green.



The blood counts of the cases presented here show that in lead poisoning there is, as a rule, only a mild type of secondary anæmia. In spite of this fact nucleated red cells may be present in the peripheral circulation. The characteristic pallor so common in patients suffering from this form of poisoning is probably referable not to the reduction of blood cells and hæmoglobin, but to some other cause, possibly a contraction of the peripheral bloodvessels.

Every case recorded in Table II. showed nucleated and granular red cells in the peripheral blood. The granular red cells were always increased in proportion to the number of nucleated cells present, and always seemed to hold a definite relation to them. Both varieties of red cells were more numerous in some cases, and decreased as convalescence was established. In many cases the intensity of the symptoms was not greater than in others, but still convalescence was much more protracted in those presenting great numbers of granular and nucleated red cells in the blood.

Vaughan, in his studies, was always able to demonstrate an increase in granular cells when there were present nucleated red corpuscles.

The constant association of the granules and nucleated red corpuscles lead me to believe that the granules are the remnants of a pre-existing nucleus, and that the three types of granulations described represent stages in the change from nucleated to non-nucleated red corpuscles. Of these probably No. 3 is the first, No. 2 the second, and No. 1 the last.

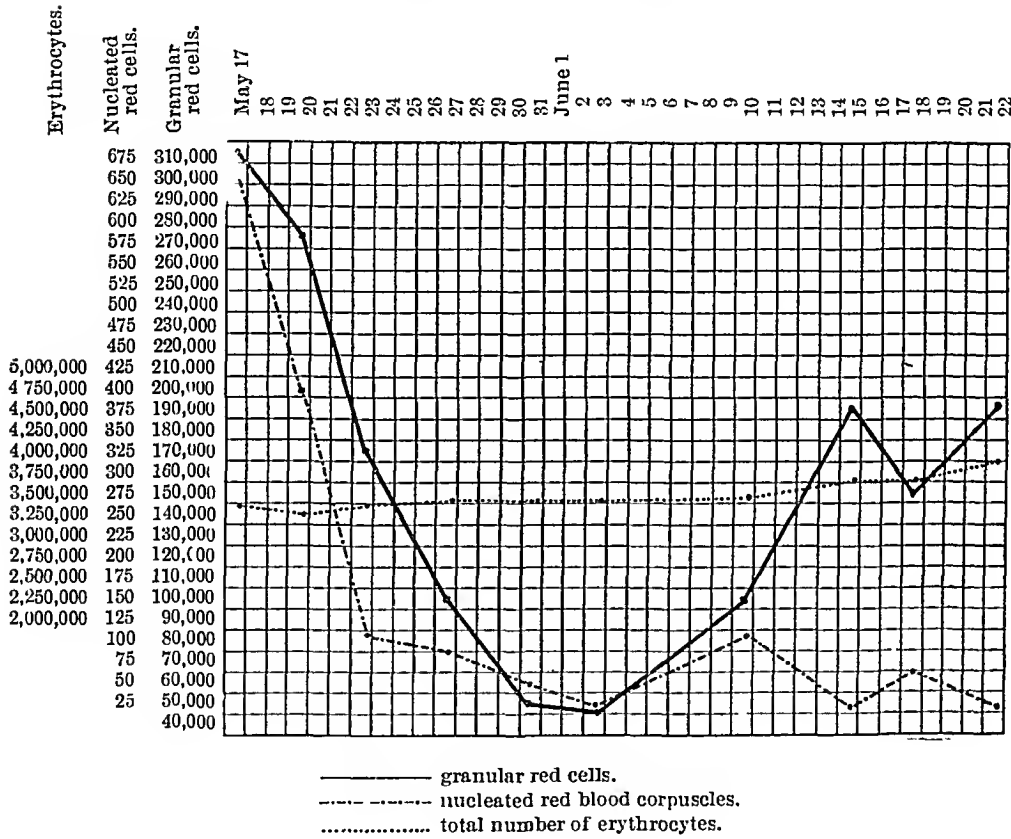
One of the arguments advanced to uphold the nuclear origin of the granules is the fact that they can only be demonstrated by means of nuclear stains. Simon, White, and Pepper have not been able to stain them with methyl green, which has always been classed as a specific nuclear stain, and thus they argue that this fact goes to prove that the granules are not of nuclear origin.

To determine this point many smears were made from cases of lead poisoning, and after brief fixation stained for five minutes with Ehrlich's methyl green and fuchsin mixture. The red cells took a very deep-red color and the granules a dark-brownish tint, so that the results were not satisfactory. A saturated watery solution of methyl green was then tried alone. Each smear was fixed for one minute at 120° C., stained one minute, and washed in water. On examining these specimens with a one-twelfth oil-immersion lens the protoplasm of the red cells appeared a yellowish color, showing no affinity for the green stain, while the nuclei of both leukocytes and normoblasts took a decided green color. The granules in the red corpuscles stained a beautiful green. (See Plate, Fig. III., *b*.) If the staining was prolonged more than one minute, the granules appeared almost black. This method of staining was carried out in all of the eleven cases shown in Table I., and in

many others. In every case the granules were easily demonstrated. The stain used was methyl green as prepared by Grüber.

Demel, in 1901, and Donati, in 1903, stated that the erythrophile and cyanophile granules in red cells were identical, showing that if one variety was not found in a given specimen of blood, the other was also absent. Marzocchi<sup>1</sup> proved the identity of these granules by substituting the red stain for the blue, and *vice versa*. He stained a drop of blood diluted with salt solution with methylene blue, and then looked for the blue granules within the red cells.

CHART I.—*Lead Poisoning.*



Then, keeping his eye on the same cell, he added a solution of neutral red in salt solution to the specimen under the cover-glass, when almost instantly the granules were seen to lose the blue and take up the red stain. The first colored fluid does not mix with the second, but flows from under the cover-glass in the opposite direction, so that the red dye is substituted for the blue.

In many cases I have been able to confirm these experiments and have succeeded in staining the granules satisfactorily by using

<sup>1</sup> Riforma Medica, January 23, 1904; quoted in New York and Philadelphia Medical Journal, February 20, 1904.

a saturated solution of neutral red instead of the polychrome methylene blue, in the method described by Vaughan. Wright's stain was also tried in this way, and although the granules could be demonstrated the results were not so satisfactory as with the polychrome methylene blue.

A series of blood counts was made in a case of lead poisoning from the wards of the hospital. This case was not more severe than the average. After being under treatment about three weeks the patient was discharged at his own request, presenting at that time no symptoms excepting marked tremors of hands. He immediately found employment (but not at his former occupation in lead works), and I was able to examine his blood during his dinner hour.

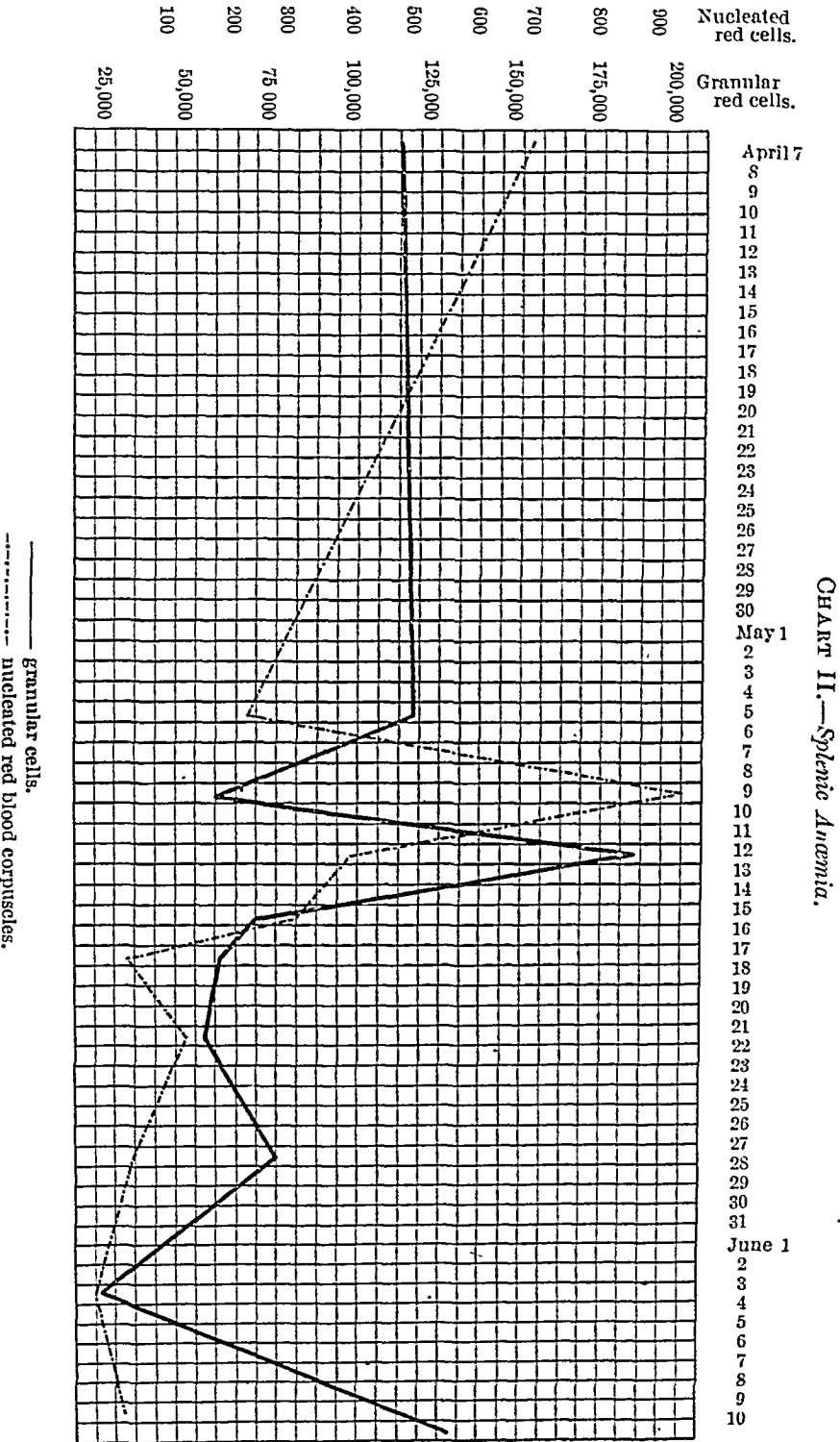
The granular cells and nucleated cells were counted as before described, and the total number of each per 1 c.mm. of blood calculated. The results of these observations are depicted in Chart I. The first count showed 650 nucleated red cells, 315,000 granular cells per 1 c.mm., while the total count of the erythrocytes was 3,496,000. It cannot be said that with such a high red count this enormous number of nucleated cells was entirely due to the anæmia.

For the first eighteen days the number of granular and nucleated red cells rapidly fell, and finally reached their lowest point while the patient was still under observation. After this there was an irregular rise and fall of both varieties of red corpuscles, the granular cells increasing rapidly just after the nucleated cells had reached their height. During all this time the total number of erythrocytes steadily increased.

Two more cases were studied in this way and results are shown in Charts II. and III. Chart II. shows the rise and fall of granular and nucleated red corpuscles in a fatal case of splenic anæmia and Chart III. is that of a severe case of pernicious anæmia.

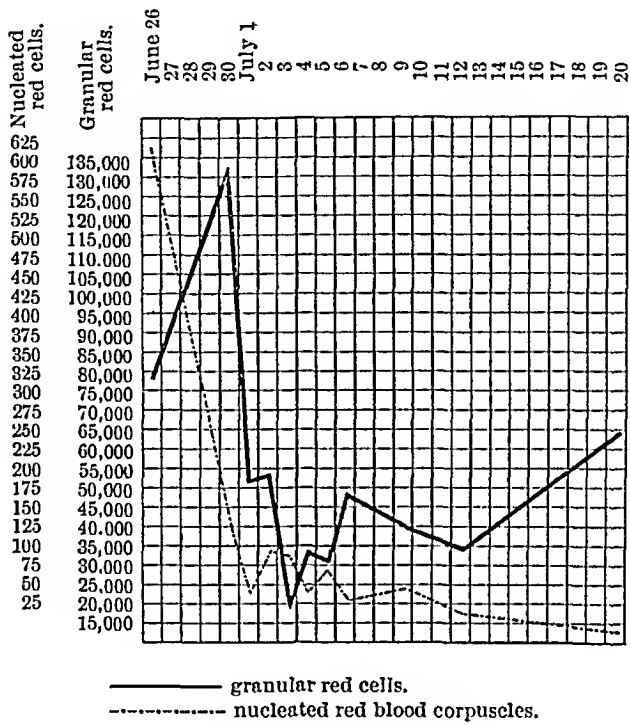
These charts are of particular interest, inasmuch as they demonstrate that the rise in granular cells follows the elevation of the nucleated red blood corpuscles. When the elevation of nucleated red blood cells is at its height, the numbers of granular cells are low, but as the nucleated red cells fall the granular cells rise. That is, the increase of granular cells is synchronous with the decrease of nucleated red blood corpuscles.

The relation which these granular cells bear to the nucleated red blood corpuscles admits of at least two explanations. It is possible that the granules represent a degeneration of the protoplasm of the erythrocytes, as suggested by Grawitz, and that this extensive and diffuse degenerative process is accountable for the expulsion of nucleated red blood cells from the hæmopoietic organs. But under these circumstances one would hardly expect the elevation of nucleated red cells to precede the rise in granular cells. On the other hand, it is conceivable, as Schmidt claims, that the



granules are derived from the nucleus of the red cells, and that in lead poisoning the presence of nucleated red cells in the general circulation is due to some toxic effect of the drug upon the hæmopoietic organs. In this event one would expect, as the charts show, that the granular cells would increase in number as the nucleated red cells decreased. Indeed, the behavior of these two types of

CHART III.—*Pernicious Anæmia.*



cells forms a strong argument in favor of the origin of the basophilic granules from the nuclei of the red blood corpuscles.

The total number of leukocytes in lead poisoning were, as a rule, normal; but many cases showed a slight decrease in the percentage of polymorphonuclear cells with an increase in the large mononuclear variety.

CONCLUSIONS.

1. Basophilic granules occurring in erythrocytes are normally present in small numbers in the blood of man, but may be increased in numbers under certain pathological conditions and decrease as convalescence is established.
2. Nucleated red corpuscles are common in the blood of those suffering from lead poisoning, and are always accompanied by an increase in the number of granular red cells.
3. The anæmia secondary to lead poisoning, as a rule, is only of a moderate degree.



4. The granular cells are most common in lead poisoning, possibly have their origin in the blood-forming tissues, and are probably the results of a fragmentation of the nucleus of the red blood corpuscle.

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## THE TOXÆMIA OF PREGNANCY.<sup>1</sup>

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AMONG the most important problems in obstetrics awaiting solution is the toxæmia of pregnancy.

The modern conception of this subject makes it responsible for eclampsia and probably for the pernicious nausea of pregnancy. We shall possibly understand better the grounds on which it is recognized if we consider briefly the modern conception of the physiology of pregnancy.

Pregnancy inevitably exposes the mother to danger. The foetus by its syncytium invades not only the tissues of the maternal body, but frequently the blood current. In health the mother's immunizing substances in her blood serum keep the growth of fetal tissue within normal limits. If this boundary be passed clinical evidence leads us to recognize the transference of syncytial substances to the mother's blood as a potent cause of syncytioma malignum, pernicious nausea of pregnancy, and eclampsia.

Pregnancy induces marked abnormalities in the metabolism of the mother. Her enlarged thyroid illustrates the necessity for the increased production of the immunizing substances furnished by this gland. The anæmia and leukocytosis of early pregnancy draw attention to alterations in her blood. Changes in the heart muscle, in the parenchyma of the liver and kidneys show the effects of altered blood condition in these important structures. Altered pulse tension gives evidence of the abnormal condition of the nervous system. These conditions are so common in pregnancy that they are not usually considered as disease and frequently pass without detection. A pregnant woman is ordinarily said to be well if she passes through gestation without its premature interruption and without eclampsia. The balance between health and disease is rarely undisturbed.

The earliest manifestation of the toxæmia of pregnancy is seen in pernicious nausea. This has long been regarded as largely of reflex nature, caused by the irritation to the nervous system of the

<sup>1</sup> Read before the Luzerne County Medical Society, November 16, 1904.

growing uterus. There seems no reasonable doubt but that the enlargement of the womb in many patients irritates the nervous system; but that this alone produces pernicious nausea or is largely responsible for it seems most unlikely, in view of the post-mortem findings. Marked changes in the liver, blood, bone-marrow and in the organs of excretion are the striking features in these cases. Ewing, of the Cornell Medical School, from a study of the changes in the liver, advances strong evidence that a toxæmic condition causes pernicious nausea. Clinical evidence supports this, for our most reliable indication of the patient's danger lies in the examination of her blood and in the presence or absence of the signs of pernicious anæmia. The most successful treatment for the pernicious nausea of pregnancy is skilful feeding and absolute rest. When these fail pregnancy must be interrupted. The correction of uterine displacement is manifestly indicated, but does not avail in severe cases. Pernicious nausea is sometimes observed in the same patient when multiple pregnancy is present, and in the same patient is absent when single pregnancy occurs. This is true at a period when the uterus is not sufficiently distended to cause marked reflex irritation. An illustration of the fact that distention of the uterus is not an essential cause in pernicious nausea is found in the circumstance that many patients with polyhydramnios escape nausea.

It may be interesting to review briefly the methods of investigation available in the study of toxæmia and their results. We are all familiar with the examination of the urine by chemicals and by the microscope. By chemistry we seek to ascertain the quantity of solids proportionately contained, the reaction of the urine and the presence or absence of substances indicating alterations in the blood. We also determine the percentage of urea, not because urea itself is a poison, but because it represents the finished product of metabolism, and is of clinical value in showing that the patient's metabolism is habitually abnormal or within the range of health. It is true that at times the percentage of urea varies widely, but the examination of specimens at regular intervals, with a knowledge of the patient's diet and hygiene, will enable the physician from the percentage of urea to gain information of value regarding her general metabolism. Chemistry also gives us information about the presence or absence of albumin, although this is of secondary importance. By the microscope we detect débris from the kidney, crystals illustrating abnormal metabolism, and also substances caused by the dissolution of the blood. The microscope is occasionally requisite to identify bacteria. By cryoscopy or the determination of the freezing point in the urine, we have a method of considerable value which enables us to estimate the concentration of the urine and to compare this with that of the blood. By the injection of urine into living animals we have a comparative test of value in ascertaining its toxicity.

Our available methods for examining the blood in these cases consist of the use of the microscope, chemical tests for the recognition of hæmatin, inoculation tests of blood serum to determine the toxicity of the blood in animals, and cryoscopy to determine the molecular concentration of the blood. We may study the mother's immunity against the syncytium by the injection of animals with placental substance. We may also by lumbar puncture extract sufficient serous fluid to enable us to study the degree of toxicity in the mother's serum. By the ophthalmoscope we may gain accurate evidence of the conditions of the small vessels as illustrated by the retina. By blood-pressure apparatus, we study graphically the mother's blood tension. The usual methods of physical diagnosis give us information concerning the heart action and the general condition of the vessels.

It is unfortunate that we possess no simple and reliable method for examining the feces. Those methods available are complicated and require expert chemical knowledge and prolonged research.

Too much importance cannot be placed upon the study of toxæmia by the patient and careful observation of the physician, without recourse to technical examination. A practitioner of experience will readily detect alterations in the patient's blood, abnormal conditions of pulse tension, evidence of impaired nutrition and excretion, and habitually altered action of the heart. The state of the mind and of the automatic portions of the nervous system can well be ascertained by clinical observation. Our modern study of this question would lead to positive injury to the profession if it caused practitioners of medicine to think that they must wait for elaborate examinations in laboratories before making a diagnosis of toxæmia. By appropriating to our use data furnished by laboratory methods, and by using these data to correct our own observations, we shall rarely fail in a correct diagnosis.

By the methods of investigation described, our best knowledge at present leads us to believe that the toxæmia of pregnancy is not essentially of nephritic origin. Numerous observations and experiments have shown that the urine is not essentially altered in molecular concentration during toxæmia and eclampsia; that the toxicity of the urine is not materially increased in toxæmia and eclampsia; that eclampsia occurs in some cases with little disturbance in the secretion of urine and without albumin; and that patients who have nephritis do not necessarily become eclamptic. It is interesting to observe that in toxæmia and eclampsia the chlorides of the urine may be greatly lessened and that the amount of water in the urine also decreases. This variation in the chlorides suggests the phenomenon seen in pneumonia, where a sudden change in the chlorides is usually regarded as evidence that the toxæmic crisis of pneumonia is passing.

While the study of the urine does not give evidence of marked

renal changes in the toxæmia of pregnancy, the examination of the blood is more conclusive. The blood serum in these cases is distinctly toxic, causing the death of animals with convulsions and with the characteristic changes of toxæmia in the important organs. The blood is lessened in its alkalescence, by some is thought to be increased in molecular concentration and to have increased crystalloid contents probably of nitrogenous origin. In eclampsia the red blood cells are greatly changed. The following striking demonstration of the condition of the blood in eclampsia and nephritis is given by Bell in cases occurring at St. Thomas' Hospital in London. A primipara eight months pregnant was admitted to the hospital in eclampsia, was delivered, developed intense jaundice, and died. Autopsy showed in the liver the characteristic lesions of intense toxæmia and the urine contained leucin. Blood serum from this patient taken before death was injected into animals and proved highly toxic, the animals dying with convulsions and characteristic lesions.

At the same time blood serum was taken from two cases of chronic nephritis in the last stages of the disease and approaching death. One was interstitial in character and the other nephritis affecting principally the convoluted tubules. The blood serum in these patients occasioned but trifling inconvenience to the animals into which it was injected, producing no convulsions and interfering with the general health of the animal very slightly.

Lumbar puncture and the examination of cerebrospinal fluid by cytology shows that the lymph cells of this fluid are markedly altered in a number of conditions in which the nervous system is primarily attacked. Thus, in cerebrospinal meningitis, in locomotor ataxia, and in rabies important changes in this fluid have been found. The number of cases of pregnant women with toxæmia in whom this fluid has been examined is as yet too small to enable us to determine the condition of the cerebrospinal fluid.

Recognizing that the poison of toxæmia is found in the blood serum, we must next question the possible source of this poison. As modern investigation has shown that the kidneys are but slightly responsible, we find that, on the contrary, the liver is the organ most frequently diseased, and that post-mortem examination shows in toxæmia most striking changes in the liver. Hemorrhagic necrosis of the liver, with multiple thrombosis, is the characteristic lesion of toxæmia and eclampsia in mother and fœtus. These lesions strikingly suggest the first stage of acute yellow atrophy. By modern pathologists, the hepatic lesions of toxæmia and eclampsia are considered so characteristic as to suggest a diagnosis from the examination of the liver only.

In the toxæmia of pregnancy, the thyroid gland is deficient or altered in activity. Lange has estimated that the gland is enlarged in 81.2 per cent. of pregnant patients. Nicholson has drawn our

attention to the deficiency of thyroid secretion in cases of eclampsia. In one of his observations, patients threatened with eclampsia placed upon milk diet were greatly improved, because the milk required but a small percentage of iodothyryn to affect the metabolism of its proteids. These patients eluded the watchfulness of their caretakers and procured pork, which they ate secretly. Eclampsia supervened. Hergot reports an interesting case of eclampsia in a cretin. Bensen draws attention to the fact that after the thyroid gland is removed in cases coming to autopsy, the renal tubules are blocked with colloid substances similar to that found in eclampsia.

In animals in which the thyroid has been removed, pregnancy has been followed by eclampsia with the birth of dead offspring. Surgeons are familiar with the fact that the removal of the entire thyroid may be followed by convulsions in animals or in the human subject. Clinically, patients threatened with eclampsia are benefited by the administration of thyroid extract.

Abundant evidence exists of the part played by the intestine in the production of toxæmia. This knowledge is so familiar that we need not delay upon this point.

We distinguish, then, in the mother, toxæmia and eclampsia of hepatic origin, of intestinal origin, of thyroid origin, and of renal origin. These are named in the order of their importance and frequency.

Our attention has also been called to the fact that the embryo or foetus may be a cause of the toxæmia of pregnancy. While we may believe that the foetus contributes somewhat to the toxins of the mother's blood, we must remember that convulsions do not cease in all cases after delivery, and that the evidence seems to show that one and the same poison affects mother and child, and not that the child originates the poison which destroys the mother. Hitschmann recently described an interesting case of pregnancy at the fifth month. The patient was seized with eclampsia and the uterus was emptied. She recovered. The womb was the size of a seven months' pregnancy; the embryo had died at about the fourth month and a placental mole had formed. In this case the death of the embryo must have been followed by a cessation in the formation of toxins from this source. Eclampsia, however, subsequently occurred. Eclampsia may occur during pregnancy and the woman recover, pregnancy be uninterrupted and a living, healthy child be born. We may, then, reasonably conclude that toxæmia and eclampsia are not to any great extent of fetal origin. It requires but a moment to observe that the efforts to prove that toxæmia and eclampsia are caused by bacteria have not been successful.

Eclampsia occasionally occurs in groups of cases. Stroganoff in St. Petersburg, Kedarneth-Das in Calcutta, and the Staff of the Edinburgh Maternity Hospital all report groups of cases in which

toxæmia and eclampsia seem an infectious epidemic. This observation has not been confirmed by others.

The effort to identify chemically the poison of toxæmia and eclampsia has not yet succeeded. Ammonium carbonate, carbamic acid, xanthin, creatin, creatinin, peptones, globulins, leucomains, ptomains, acetones, and urobilin have all been studied as possible causes of this condition. None of these is proven to cause toxæmia or eclampsia. Some have believed that toxæmia is accompanied by increased excretion of ammonia, while the theory that nitrogen is deficiently excreted has long received attention.

Syneytiolisin, a placental ferment, undoubtedly influences the blood of the mother, and probably has something to do in the causation of eclampsia. Its mode of action consists in causing solution of blood corpuscles, thus favoring the production of thrombi. Extract of human placenta injected into animals causes the animals to perish in spasms and with great prostration. The toxicity of placental extract varies with the maternal condition. In some fatal cases of eclampsia, syncytial tissue has been found growing on the peritoneum and ovaries.

From these considerations, can we deduce knowledge of a practical nature concerning the detection of toxæmia and the prevention and treatment of eclampsia? Remembering that toxæmia is more than renal insufficiency or nephritis, our scrutiny of the patient must go farther than the examination of the urine. Sufficiently often the patient must be seen by her physician and her condition noted. The nervous system gives especially valuable indications of toxæmia. Headache, altered secretion and excretion, neuralgia, unusual mental conditions, increased vasomotor stimulation and high pulse tension, disturbances in the sensory apparatus, all indicate toxæmia. Altered secretions, obstinate constipation, jaundice, and signs of disintegration of the blood are of especial importance.

In the treatment of this condition, the details of hygiene must be thoroughly carried out. The diet should be regulated, and indigestible and highly nitrogenous food reduced to a minimum or entirely omitted, and fresh, sound milk substituted. The free use of fruits and green vegetables in season is also indicated. Water taken between meals, before retiring, and upon rising is a common prescription often difficult of execution. The avoidance of alcohol and of large quantities of alkaloidal stimuli is of great importance. Fresh air, regular bathing, sufficient sleep, proper clothing, and reasonable exercise all are most important. So common are these precautions that they are frequently neglected.

So far as drugs are concerned, laxatives are indicated. In the presence of acute toxæmia, it must be remembered that salines often cause the dissolution of dried feces and the prompt absorption of fecal matter. To increase the solid excretion of the body, calomel

is of decided value. To act as a powerful diuretic and to stimulate some of the necessary processes of nutrition, thyroid extract has proven efficient. No greater mistake can be made than to treat the neuralgia or sleeplessness of toxæmia by the administration of sedatives or narcotics. This is but adding fuel to the flames. What is needed in these cases is oxygen, purgatives, stimulation of the skin, a selected diet, and abundant rest.

In the presence of persistent and increasing toxæmia which does not yield to treatment, the question of the induction of labor naturally arises. It must be kept in mind that the artificial termination of pregnancy often brings with it shock to the mother and in many cases increases her toxæmia. If she be suitably cared for, nature will usually adjust the question of pregnancy by allowing gestation to continue or by bringing about changes in the placenta which will result in the death of the child. This course is safe for the mother, although less prompt than the induction of labor.

Of especial value in preventing serious toxæmia is the use of saline waters, and of these Vichy is of especial advantage. In the presence of threatening toxæmia, the free use of normal salt solution by hypodermoclysis or by rectal injection is especially indicated. The use of the hot pack or bath requires caution, for the temporary increase in pulse tension following the beginning of the bath or pack may induce eclampsia; hence the physician must be prepared to administer veratrum viride hypodermically should the pack increase the tension of the pulse.

We cannot remember too clearly the fact that in the toxæmia of pregnancy the vital organs of the patient are undergoing extensive degenerative changes. Cloudy swelling and fatty degeneration of the heart muscle, minute hemorrhages in the substance of the liver, spleen, and lungs, and serous effusions or inflammations seriously threaten the patient's life. The toxæmic woman is not safe with the termination of pregnancy, for she may pass through eclampsia only to perish from pneumonia, cardiac syncope, pernicious jaundice, or general debility. Eclampsia is but a step in the march of the toxæmic process, marking its acutest attack, but not guaranteeing the patient against further disease.

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## THE CLINICAL MANIFESTATION OF HEMORRHAGES IN ECLAMPSIA.<sup>1</sup>

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HEMORRHAGIC manifestations in eclampsia are fortunately very rare, for they are evidenced only in those cases suffering from an extreme degree of toxicity—so extreme, indeed, that death is usually the outcome. Why, of two cases of eclampsia, of apparently equal intensity, the one should develop this hemorrhagic condition and the other should not, we cannot as yet say, for in both cases the liver may be apparently involved to an equal degree.

The same manifestations may likewise occur in severe cases of toxæmia of both pregnancy and the puerperium; but of these it is not my purpose to speak at this time.

**FREQUENCY.** After an extensive review of the literature on eclampsia, no accurate conclusion has been reached by the writer as to the frequency of this group of cases. It is so rare, however, that only a few isolated cases have so far been reported, and that not one of the usual text-books on obstetrics speaks of it as even existing. Newell, reviewing 78 cases of eclampsia under his care up to 1899, does not mention a single case of this type.

In studying the series of eclamptics at the Sloane Maternity Hospital (up to August 15, 1904), we find that in the last 12,000 deliveries there were 152 cases of eclampsia. Of these 152 cases, apparently only 7 (*i. e.*, 4.6 per cent., approximately) gave clinical evidence of hemorrhages. Of these 7 cases, 5 occurred during the past two years.

Owing to the unusual character of this type of eclampsia, we beg leave to present to you the following cases taken from the series just mentioned, and in so doing we shall endeavor to omit all details not pertinent to the question in hand:

**CASE I.** (History No. 14,290).—The patient, a colored I-gravida, aged twenty-six years, was admitted to the hospital in an unconscious state, with marked albuminuria. The onset of the disease was a sudden one. Soon after admission she delivered herself of a small, premature infant of about six months. One hour after labor she had a severe convulsion. Despite the usual active medical treatment, there were twelve more convulsions during the next twelve hours. Temperature, 100°; pulse 84 to 100.

**Uranalysis.** Total quantity, 13½ ounces; specific gravity, 1044; reaction acid; 90 per cent. albumin by boiling and centrifuge; urea, 160+ grains; many casts of all of the common varieties.

<sup>1</sup> Read before the Society of the Alumni of the Sloane Maternity Hospital, October 28, 1904.

*First Day Post-partum.* Marked general improvement during night. Patient at times conscious, taking some nourishment. During the day she was quiet; toward evening, however, became restless. The abdomen became distended and tender. There was some jaundice of the scleræ. Temperature,  $100.8^{\circ}$  to  $99.8^{\circ}$ ; pulse, 130 to 88.

*Uranalysis.* Total quantity, 8 ounces; specific gravity, 1040; acid; 50 per cent. albumin, centrifuge; urea, 96+ grains in twenty-four hours.

*Second Day Post-partum.* No convulsions; delirious at times; severe abdominal pain and marked abdominal distention. Great tenderness over the liver, but the latter did not seem changed in size.

Toward the middle of the day the patient began to vomit coffee-ground material—this vomiting soon becoming almost continuous. Despite all efforts, death occurred in the early evening. Temperature,  $97^{\circ}$ ; pulse, 90 to 100.

*Uranalysis.* Total quantity, 11 ounces; 5 per cent. albumin, centrifuge; urea, 1.9 grain to 1 ounce (total quantity of urea, 20.9 grains); many hyaline and granular casts. Lochia normal throughout.

CASE II. (History No. 14,310).—Patient, a white I-gravida, aged nineteen years, six months along; was brought to the hospital in a semicomatose condition, with the history of having had several convulsions. The previous renal history was negative.

On admission she was found to be markedly œdematous and markedly toxic. An accouchement forcé was performed within a few hours.

*Uranalysis on Admission.* Acid; specific gravity, 1030; 60 per cent. albumin, centrifuge; urea, 6.2 grains to the ounce; many casts. Temperature,  $101^{\circ}$ ; pulse, 120.

*First Day Post-partum.* Semicomatose; no convulsions; general condition much better apparently. Temperature,  $99^{\circ}$ ; pulse, 90 to 70.

*Uranalysis.* Total quantity, 10+ ounces; specific gravity, 1040; acid; 20 per cent. of albumin by centrifuge; 88+ grains of urea in twenty-four hours; many casts.

*Second Day Post-partum.* Rational at times, but restless; pain in abdomen and some distention; milk and water well taken. Temperature,  $99.4^{\circ}$  to  $100^{\circ}$ ; pulse, 90 to 120.

*Uranalysis.* Total quantity, 32 ounces; specific gravity, 1010; acid; 5 per cent. of albumin by centrifuge; urea, 95 grains in twenty-four hours; many casts.

*Third Day Post-partum.* Conscious, but unreasonable; more abdominal distention; increased pain and tenderness, especially over the liver; jaundice; vomited 12 ounces of coffee-ground material. Temperature,  $100.4^{\circ}$  to  $99.4^{\circ}$ ; pulse, 90 to 120.

*Uranalysis.* Total quantity, 50 ounces; specific gravity, 1012; acid; trace of albumin; urea, 70+ grains in twenty-four hours; few casts.

*Fourth Day Post-partum.* Severe headache; frequent vomiting throughout the day of coffee-ground material in considerable quantities. Temperature, 98°; pulse, 100 to 120.

*Uranalysis.* Total quantity, 32 ounces; specific gravity, 1034; 5 per cent. of albumin, centrifuge; urea, 265 grains in twenty-four hours; more casts.

*Fifth Day Post-partum.* More vomiting of coffee-ground material during night. Gradual improvement during day. Less pain and less abdominal distention. Temperature, 98° to 99.8°; pulse, 124 to 100.

*Uranalysis.* Total quantity, 22 ounces; specific gravity, 1034; 5 per cent. of albumin, centrifuge; urea, 150 grains in twenty-four hours; some casts. From this time on gradual, steady improvement. Discharged on the twenty-second day. Lochia normal throughout.

CASE III. (History No. 14,699).—Patient, a white I-gravida, aged thirty-two years, about eight and a half months along; was admitted to the hospital with severe albuminuria. As her symptoms became steadily worse under medical treatment, labor was induced six days later. An accouchement forcé was performed after slight preliminary dilatation of the cervix with a Voorhees bag. During labor patient had two convulsions; then became quiet and rational. During the days of the medical treatment alone, the albumin increased from 4 per cent. to 8 per cent. by centrifuge; and the urea changed from 5 grains to the ounce to 2 grains to the ounce. The total quantity of urine ranged from 35 to 26 ounces per day.

*First Day Post-partum.* Restless, but no convulsions; general condition very poor. Lower part of abdomen very painful. Temperature, 97.4° to 99°; pulse, 140 to 120; respirations, 26 to 36.

*Uranalysis.* Total quantity, 18 ounces; specific gravity, 1030; acid; 3 per cent. albumin, centrifuge; urea, 145 grains in twenty-four hours; no casts.

*Second Day Post-partum.* Restless; nauseated; abdomen distended and painful; jaundiced; vomited throughout the day small amounts of coffee-ground material. Toward evening, marked tenderness over liver and stomach. Temperature, 98° to 99.6°; pulse, 120.

*Uranalysis.* Total quantity, 43 ounces; specific gravity, 1020; acid; 3 per cent. albumin, centrifuge; urea, 495 grains in twenty-four hours; many casts.

*Third Day Post-partum.* Vomiting of coffee-ground material continues; apathetic; some slight enlargement of the liver. Temperature, 98.4° to 99.4°; pulse, 120 to 140.

*Uranalysis.* Total quantity, 26 ounces; specific gravity, 1020; acid; 1 per cent. albumin, centrifuge; urea, 255 grains in twenty-four hours; no casts.

*Fourth Day Post-partum.* General condition much worse; very weak; vomited large amounts of old blood. No response to stimulation. Died 5 A.M. Temperature had ranged between  $98.8^{\circ}$  to  $100.4^{\circ}$ ; pulse between 140 and 120. Lochia normal throughout.

CASE IV. (History No. 14,916).—Patient, a white I-gravida, aged twenty-five years, five months along; was admitted in an unconscious state, having had several convulsions. She was delivered ten hours later by an accouchement forcé (the cervix required preliminary softening). No convulsions during labor. General condition fair.

Temperature,  $101^{\circ}$  to  $102.2^{\circ}$ ; pulse, 110 to 138. Leukocytes, 62,000.

*Uranalysis.* Total quantity, 8 ounces; acid; solid with albumin; urea, 70 grains; many casts.

*First Day Post-partum.* Color poor; jaundiced; restless; several convulsions; abdomen distended and painful. Leukocytes, 88,600. Marked apparent improvement toward evening. Temperature,  $102.8^{\circ}$  to  $98^{\circ}$ ; pulse, 140 to 120.

*Uranalysis.* Total quantity, 18 ounces; specific gravity, 1022; 3 per cent. albumin, centrifuge; urea, 155 grains in twenty-four hours; many casts.

*Second Day Post-partum.* General condition suddenly grew worse; two short convulsions; abdomen markedly distended and painful. Hepatic region tender; early in the day vomited blood-streaked fluid; stools became tarry. In the early afternoon vomited bright-red blood and died shortly afterward. Temperature,  $101.6^{\circ}$  to  $98^{\circ}$ ; pulse, 140 to 150; leukocytes, 36,200 (marked drop). Lochia normal throughout.

CASE V. (History No. 8925).—Patient, II-gravida, aged twenty-four years, six and a half months along; walked into the hospital complaining of headache and dizziness. She had been sick for two days, and had had two convulsions at her home on the day of admission. She looked badly infected.

*Uranalysis on Admission.* Seant; specific gravity, 1032; boiled solid with albumin; many casts. Labor was at once induced. She was delivered on the following day. Temperature,  $99^{\circ}$ ; pulse, 110.

*First Day Post-partum.* No convulsions, but severe headache. Toward evening some abdominal pain and distention; vomited some coffee-ground material.

*Uranalysis.* Total quantity, 47 ounces; acid; 50 per cent. albumin by boiling; many casts. Temperature,  $98^{\circ}$ ; pulse, 100 to 80.

*Second Day Post-partum.* Restless, noisy; one severe convulsion; markedly jaundiced; vomited in the course of the day this same coffee-ground material. Hemorrhage into skin near vulva. Temperature,  $98.8^{\circ}$  to  $103.2^{\circ}$ ; pulse, 100 to 80.

*Uranalysis.* Total quantity, 17 ounces; acid; specific gravity, 1018; 8 grains of albumin after boiling, by centrifuge.

*Third Day Post-partum.* Semicomatose; condition not so good; marked pain and tenderness over liver. Vomited coffee-ground material and some bright-red blood. Temperature, 98° to 99°; pulse, 80 to 94.

*Uranalysis.* Total quantity, 10 ounces; specific gravity, 1012; 8 per cent. of albumin; no casts.

*Fourth Day Post-partum.* Condition about the same, but no vomiting.

*Fifth Day Post-partum.* Still tenderness over liver; no vomiting; tarry stools.

*Uranalysis.* Total quantity, 8 ounces; 5 per cent. of albumin; specific gravity, 1086; no casts. Temperature, 98°; pulse, 84 to 90.

*Sixth Day Post-partum.* Feels somewhat better; tarry stools continue.

*Uranalysis.* About the same. Temperature, 98° to 100°; pulse, 90 to 110.

*Seventh Day Post-partum.* Very stupid and drowsy; very marked abdominal distention; frequent loose, dark, tarry stools.

*Eighth Day Post-partum.* No vomiting; stools the same.

*Ninth Day Post-partum.* Condition the same.

*Tenth Day Post-partum.* Subcutaneous ecchymoses on back and chest. Patient much weaker; deeply comatose. Temperature, 98.8°; pulse, 120.

*Uranalysis.* Total quantity, 6½ ounces; 3 per cent. of albumin; casts.

*Eleventh Day Post-partum.* Death early in the morning. Lochia normal throughout.

CASE VI. (History No. 12,780. Reported in *Medical News*, November 21, 1903).—Patient, a white I-gravida, aged twenty-two years, six and a half months along; entered the hospital with a rather severe albuminuria. She had only had symptoms for three days.

*Uranalysis.* Scant; specific gravity, 1026; 30 per cent. of albumin by boiling; many casts; urea, 5 grains to the ounce. She was placed at once on medical treatment. About three hours after admission she had a severe convulsion. An accouchement forcé was performed, which was well borne by the patient. She slept quietly most of the night. When awake, nourishment was well taken. Temperature, 99.8°; pulse, 84; respiration, 24.

*First Day Post-partum.* Severe frontal headache; moderate nausea and vomiting; restless, but no convulsions. Nourishment fairly well taken. Temperature, 99° to 97.8°; pulse, 80 to 100, of moderate tension.

*Uranalysis.* Acid; specific gravity, 1016; albumin, 5 per cent. by centrifuge; urea, 150 grains in twenty-four hours; many hyaline and granular casts; total quantity, 50 ounces.

*Second Day Post-partum.* Nauseated; vomited several times dark-brown fluid; abdomen distended, painful, and tender. Tenderness

especially marked in the right hypochondrium. Moderate jaundice; oedema of the face; expectorated bright-red blood in the evening, and complained of a severe pharyngitis. Pharynx congested. Temperature, 98.4°; pulse, 110 to 120, of high tension.

*Uranalysis.* Acid; specific gravity, 1018; albumin, 2 per cent., centrifuge; urea, 50+ grains in twenty-four hours; moderate number of hyaline, granular, and epithelial casts; total quantity, 24 ounces.

*Third Day Post-partum.* Frequent vomiting of dark-brown fluid; abdomen somewhat less distended and tender; fair result from strong catharsis; jaundice the same; many petechial spots on trunk and extremities; pharynx very painful; submucous retropharyngeal hæmatoma. Some general improvement toward evening. Temperature, 98° to 100.2°; pulse, 130 to 120, irregular at times and of moderate tension.

*Uranalysis.* Acid; albumin, 2 per cent., centrifuge; urea, 488 grains in twenty-four hours; many hyaline and granular casts; total quantity, 61 ounces.

*Fourth Day Post-partum.* No headache; less irritable and restless; pharynx the same; vomited dark-brown fluid; abdomen moderately distended and tender; no enlargement of the liver. Temperature, 100° to 98.4°; pulse, 128 to 100, of low tension.

*Uranalysis.* Acid; specific gravity, 1024; albumin, 1 per cent. by centrifuge; urea, 485 grains in twenty-four hours; casts of all varieties; total quantity, 69 ounces.

*Fifth Day Post-partum.* General condition apparently improved; pharynx improved; no vomiting; blood-stained fluid defecation. Temperature, 98.4° to 100.2°; pulse, 118 to 114.

*Sixth Day Post-partum.* Nauseated; vomited dark-red blood several times; severe epigastric pain; abdomen tender and somewhat distended; jaundice the same; no headache; restless. Temperature, 100.6° to 100°; pulse, 124 to 112; respirations, 28 to 38.

*Uranalysis.* Acid; specific gravity, 1024; albumin, 2 per cent. by centrifuge; urea, 475 grains in twenty-four hours; casts decreasing; total quantity, 53 ounces.

*Seventh Day Post-partum.* Jaundice less; pharynx no longer painful; hæmatoma decreased in size; tarry stools; general improvement toward evening. Temperature, 100.4° to 100.6°; pulse, 120 to 110. Lochia normal.

*Eighth Day Post-partum.* No headache; no restlessness; cheerful; no abdominal pain and only slight distention; vomited small amount of blood; stools normal. Slight odor to lochia. Temperature, 100.8° to 100°; pulse, 112 to 118.

*Uranalysis.* Acid; specific gravity, 1024; albumin, 1 per cent. by centrifuge; urea, 225+ grains in twenty-four hours; total quantity, 25 ounces; only few casts.

*Ninth Day Post-partum.* Marked general improvement; jaundice and petechial spots have almost disappeared; abdomen soft;

nourishment well taken. Lochia normal. Temperature, 101° to 99°; pulse, 110 to 120; respirations, 28 to 32. From this time on the patient made an uninterrupted recovery. There were no further hemorrhages. The albumin and casts gradually disappeared. The temperature, which was in part due to some slight uterine absorption, gradually dropped to the normal. The patient was discharged on October 19th in a very fair condition.

**CHIEF SYMPTOM-COMPLEX.** In analyzing critically the above cases, we find a group of symptoms that are most striking, that are quite characteristic of this type of eclampsia, and quite unlike any other form of the disease. These symptoms are:

1. *The profound toxicity.*
2. *The jaundice.* This is far more constant and more marked than in the ordinary type of case. It was present in all of our cases under discussion.
3. *The abdominal distention.* This is usually both a prominent and an early symptom, and is at times most distressing. It begins as an epigastric distention, which then gradually becomes generalized. This sign is of bad omen, and in every case of eclampsia, if it develops, we should be on the watch for hemorrhagic complications.
4. *The vomiting.* This consists of clear fluid or curdled milk; then of bile; and finally of coffee-ground material or of clear blood.
5. *The pain and tenderness over the liver.* These are often of great intensity.

6. *Hemorrhagic manifestations* other than the vomiting of blood.

**PATHOLOGY.** The chief pathological features of the cases under consideration, as well as of the severer cases of eclampsia, without the clinical manifestation of hemorrhages, are:

1. The development of multiple hemorrhagic foci in the various organs.
2. The development of thrombotic processes in many of the smaller vessels.
3. The formation of irregularly shaped areas of necrosis in the several organs of the body, especially in the liver, these necrotic areas being largely dependent upon the thrombi mentioned above. These thrombi are at times recognizable with the naked eye; more often they are not. They are not artefacts, nor are they placental-cell emboli, as they were at one time thought to be. They consist mainly of hyaline material.

*The Brain.* The brain shows macroscopically, according to Prutz, œdema in 42 per cent. of cases, hyperæmia in 30 per cent., apoplexy in 3 per cent., a normal condition in 10 per cent. of the cases; microscopically, many small areas of necrosis are to be found, depending largely upon a mild thrombosis in the smaller vessels.

*The Heart.* The myocardium shows marked parenchymatous degeneration, also many small foci of necrosis, which may be due both to the toxæmia and to prolonged use of chloroform.

*The Liver.* The liver is usually but little changed in size, and the capsule smooth. There may be found beneath it hæmatomata of varying size (4 cases have been reported that ruptured fatally into the peritoneal cavity). Both the surface of the organ, as well as its substance, are moderately icteric. We note, further, irregularly shaped red and yellow areas scattered throughout its substance and on its surface.

Microscopically, these areas are found to consist of hemorrhagic and anæmic necroses, which may or may not contain red blood cells. These necroses have a tendency to lie near the periphery of the lobules, and are now considered to be largely the result of thrombotic processes which are found in the smallest radicles of the portal vein, very occasionally in the radicles of the hepatic artery.

The necrosis is essentially a coagulation necrosis, accompanied by an unusually large amount of fibrin.

There may be definite hemorrhage into the substance of the liver, apart from the hemorrhagic necroses.

Such is the common picture of the liver in fatal cases of eclampsia. Bouffe de St. Blaise demonstrated these lesions in 42 consecutive cases; Schmorl found them in 71 out of 73 autopsies. These results have been attested to by many other observers, as well as by myself. In rare instances we find the typical picture of "acute yellow atrophy," viz., the liver is much reduced in size; the capsule wrinkled; the degeneration most intense, and especially marked in the mid-zonal areas.

*The Kidneys.* These show most frequently an acute nephritis, with marked necrosis of the renal epithelium. This acute process is occasionally grafted upon a chronic one.

Prutz found renal changes in all but 7 out of 368 cases. The frequency of renal involvement was attested to by Schmorl, Lubarsch, and others.

Despite these findings, Prutz's conclusions are stated as follows: "Notwithstanding the frequency of renal changes, we are not justified in the majority of cases in considering them as the anatomical substratum of eclampsia, for in many instances they are too insignificant."

Bouffe de St. Blaise states that in many cases the kidneys show almost a normal condition, while Winkler, Knapp, Pels Leusden believe the renal changes to be the most important.

*The Ureters.* These were found by Prutz to be dilated in 38 out of 500 autopsies.

*The Stomach and Intestines.* These are found to contain more or less free blood; there may be actual erosions of the mucous membrane or merely punctate hemorrhages, with or without necrotic areas. In 2 cases reported, sudden death occurred from hemorrhage due to an actual ulceration of the stomach.



*The Mesentery.* This contains many punctate hemorrhages, with some thromboses in the finer capillaries.

*The Spleen.* The spleen is usually not enlarged or only slightly.

*The Blood.* The blood shows a leukocytosis in the majority of cases; little or no change in the red blood cells; a lessened alkalinity; no change in the toxicity; a normal molecular concentration. The chemistry is still so unsettled that no consideration of it will be made at this time.

*The Urine.* The urine shows an early decrease in quantity; a high specific gravity; usually a decrease in the urea; the presence, in most cases, of large amounts of albumin and large numbers of casts; but little change in the molecular concentration. Leucin and tyrosin are occasionally present.

From the pathological anatomy, then, we find that although the kidneys show changes in a large percentage of cases, still these changes do not seem to be so uniformly severe nor so uniformly present as the changes in the liver. Further, it seems to the writer that the disease called eclampsia presents a fairly characteristic pathological picture differing, on the one hand, with acute atrophy of the liver, and, on the other, with the usual acute degenerations. We do not believe that we should speak of eclampsia as being either primarily renal or primarily hepatic in origin; but that we should regard the lesions in both liver and kidneys as the result of and not as the cause of a toxæmia, the true nature of which is not as yet known, but a toxæmia in which undoubtedly both mother and foetus play a part.

**PROGNOSIS.** The prognosis of the type of case under discussion is a very poor one. Five of our 7 cases died—*i. e.*, a mortality of 70+ per cent., as against 17+ per cent. in the general series of eclamptics during the past four years at the Sloane Maternity Hospital.

**TREATMENT.** 1. Sedatives; emptying the uterus; diuresis, etc.

2. Suprarenal extract and calcium chloride in large doses, preferably given per rectum.

**NOTE.**—I wish to express my thanks to Dr. Edwin B. Cragin for granting me the use of the material in the wards of the Sloane Maternity Hospital.

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## PATHOLOGICAL STUDY OF A CASE OF MYXŒDEMA ASSOCIATED WITH TUBERCULOSIS OF THE ADRENALS:

WITH REMARKS ON THE NERVOUS SYSTEM.<sup>1</sup>

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THE following report embodies the results of the pathological study of a typical case of myxœdema.

The disease had been gradually progressing during a period of four years, so that the dermal and neural manifestations were well marked at the time of death.

<sup>1</sup> Presented, with specimens, at a meeting of the New York Society of Internal Medicine, October 19, 1901.

Especial care was devoted to the study of the nervous system, without discovering any lesion which might serve as an anatomical basis.

Of unusual interest was the coexistence of an extensive chronic tuberculosis of the adrenal glands, unaccompanied by the symptoms of Addison's disease.

*Summary of Case.* A woman, aged fifty-one years, with well-marked nervous and cutaneous symptoms of myxœdema. Insidious onset and gradual progression. Duration four years. Death from purulent bronchitis with beginning bronchopneumonia. Autopsy: The thyroid gland was sclerosed and atrophied. The hypophysis cerebri slightly enlarged. Both suprarenal glands were the seat of extensive chronic tuberculosis. The histological examination of the central and peripheral nervous systems was entirely negative. There was well-marked generalized arteriosclerosis.

*History.* Admitted to Bellevue Hospital, service of Prof. Dana, April 3, 1901. The patient was a married woman, aged fifty-one years, a native of Vienna, immigrating to this country fifteen years ago. Until four years ago she had worked in a silk factory. Her parents died of old age. She has four sisters and one brother, none of whom suffered from goitre or disease similar to her own.

Of four children two are living and in good health, one died the result of an accident, and one of chronic hydrocephalus. The previous history throws no light on her present trouble. She had been singularly free from any illness, this being the first time she had taken to her bed. The catamenia ceased with her forty-second year. Until then the menstruations had been regular and normal.

Habits as regards alcohol, tea, and coffee were moderate, and there were no grounds for suspecting a luetic affection.

The first symptoms of the disease from which she now suffers date back four years, consisting of headaches, chiefly occipital, and vertiginous seizures. She became weak and was forced to abandon her occupation, and the hair which had never been very thick commenced to fall out. A year later the face became swollen, especially about the eyes, and persisted (Figs. 1 and 2). The legs would also swell; this, however, was inconstant and was brought on by standing and walking, disappearing in the recumbent posture. During the past three years micturition has been abnormally frequent, requiring her attention several times during the night.

The headaches continued and are growing more severe, and the vision has been failing for a year. This, with the profound weakness, brings her to the hospital.

*Status Præsens.* The patient is of medium height, heavily built and very corpulent. She is singularly dull and apathetic and extremely slow in thought and action.

The hair of the head is coarse in texture, of a dull yellowish-brown color and very sparse. Over the top and sides of the head are areas of alopecia.

FIG. 1.



Myxœdematous deposits in the face, neck, and hands.

FIG. 2.



Loss of hair and alopecia in myxœdema.

The skin and subcutaneous tissue of the face, neck and hands are swollen and œdematous in appearance. The nose is broadened, the lips thick, the eyelids puffed and swollen, narrowing the interpalpebral fissure.

These areas of subcutaneous swelling are firm and elastic to the feel, not pitting on pressure.

The tongue is enlarged and presents a swollen appearance.

The skin of the body is dry and over the hands, forearms, feet, and legs it is quite harsh, with a tendency to scaling. The nails, with the exception of longitudinal ridging, are well preserved.

The cheeks are of a slight rosy tint, due to capillary infection and in marked contrast to the surrounding skin, which is of a yellowish, waxy hue.

The pupils are equal, responding promptly to light and accommodation.

The gross motor power, apart from great general weakness, is unimpaired.

With the exception of a blunting and a retardation there are no objective sensory disturbances.

The tendon reflexes of the lower extremities are present. Plantar flexion of the toes on stimulating the sole of the foot.

The acuity of both sight and hearing is impaired, but no gross defect is demonstrable.

The patient can stand without assistance and with the eyes closed.

The gait is extremely slow and labored, and awkward almost to inco-ordination. The slightest exertion is followed by fatigue. She complains frequently of the cold, although well clothed and in a ward of comfortable temperature.

The speech is slow and monotonous in character. Perception is very slow and a well-marked interval separates the answer and the question. The answers are, however, clear, expressing comprehension and some intelligence, but are expressed in a slow, monotonous fashion.

The memory for events of the distant past is not seriously impaired. The patient can recall with comparative ease incidents which transpired in Vienna twenty-five years ago, while happenings of recent origin have escaped her entirely.

Her mental attitude is one of apathetic complacency and torpor. She takes very little heed of her surroundings and sleeps a great deal. She is always dozing off; this happens while in conversation and at meals. Nothing seems to arouse her from this state of lethargy.

She has no hallucinations and no delusions and is neither suspicious nor irritable.

The condition of the thyroid gland cannot be determined by palpation owing to the swelling of the subcutaneous tissues at the base of the neck.

*Heart.* There is a moderate hypertrophy of the left ventricle with accentuation of the second aortic sound.

The pulse is full, of normal frequency, with moderate increase of the tension.

*Urine.* April 4, 1901: specific gravity, 1022; acid, large trace of albumin; no sugar. April 9, 1901: acid, 1013; albumin, 0.2 per cent., a few hyaline and granular casts.

*Blood.* Red cells, 5,112,000; white cells, 7000; hæmoglobin, 90 per cent. The differential count was normal.

*Temperature.* The temperature curve from April 3 to April 12 ranged between 98° and 99°. At no time was it subnormal. On April 12th the temperature rose to 101°, with the appearance of numerous rales over both lungs. Later cyanosis of the lips and finger-tips. Rapid, feeble pulse, hurried respiration. Death, April 21, 1901, eighteen days after admission.

*Post-mortem Examination.* The autopsy was performed by Dr. E. S. Thayer twenty-seven hours after death. Rigor mortis is well marked, muscular tissue is pale, and the subcutaneous tissue is thickened and firm. Heart is enlarged, weighs one pound, and the muscle is pale and flabby. The free borders of the mitral valve are moderately thickened, as are likewise some of the attached chordæ tendineæ.

The aortic cusps are sclerosed and in the neighborhood of their attachment adherent and thickened.

The arch of the aorta is the seat of numerous plaques of atheroma. Arteriosclerotic patches are also present in the coronary arteries. Both ventricles are hypertrophied and somewhat dilated. Beneath the pericardium a small subserous hemorrhage is visible. The pericardial sac contains 150 c.c. of clear serum.

The lungs are congested and oedematous, especially on the right side. The bronchi are filled with purulent secretion.

*Adrenals.* Both of the suprarenal capsules are considerably enlarged, firm and of a pale-yellow hue. The surface of section shows areas of cheesy degeneration, calcareous infiltration, with scattered islets of adrenal tissue. Kidneys are slightly enlarged. Capsule not adherent. The surface is irregular and cicatricial and contains scattered retention cysts. The cortex is swollen; markings well preserved.

Liver weighs four and one-half pounds. Surface of section dark and congested, otherwise normal.

Spleen weighs ten ounces. The capsule is thickened and adherent to surrounding parts. Surface of section congested, with moderate increase of the connective tissue.

The tongue is enlarged and the adenoid tissue at the base of the tongue and pharynx is hypertrophied.

*Thyroid gland* is reduced in size about one-half, is of a yellowish-white appearance and of firm sclerotic consistency. On section the

surface presents but little resemblance to the normal gland. It is yellowish-white, of fibrous texture, with scarcely any sign of glandular tissue or colloid.

Uterus and appendages save congestion of the mucous membrane and cystic degeneration of one ovary are normal.

Brain, spinal cord, and peripheral nerves, except a moderate œdema of the cerebral pia mater and arteriosclerosis of the circle of Willis, show no gross pathological changes.

Pituitary body was slightly enlarged and hyperæmic.

*Microscopic Examination. Thyroid Gland.* Both lobes and the isthmus are atrophied and the seat of extensive sclerotic changes. The connective increase is greater in the peripheral portion of the gland, especially beneath the capsule, which is considerably thickened. There is scarcely any trace remaining of the normal structure of the acini with their colloidal contents. Here and there are a few miniature acini lined by flattened epithelium and containing small disks of colloid (Fig. 3).

FIG. 3.



Atrophy and sclerosis of thyroid gland. Atrophic acini containing minute disks of colloid.  
Hæmatoxylin and eosin.

Many of these glandular remnants are composed of dense masses of epithelial cells, broken up by connective tissue into columnar and tubular groups, and resembling foetal thyroid structure. Some of these groups undoubtedly represent a compensatory regeneration of the glandular elements, while others are simply compressed and obliterated follicles.

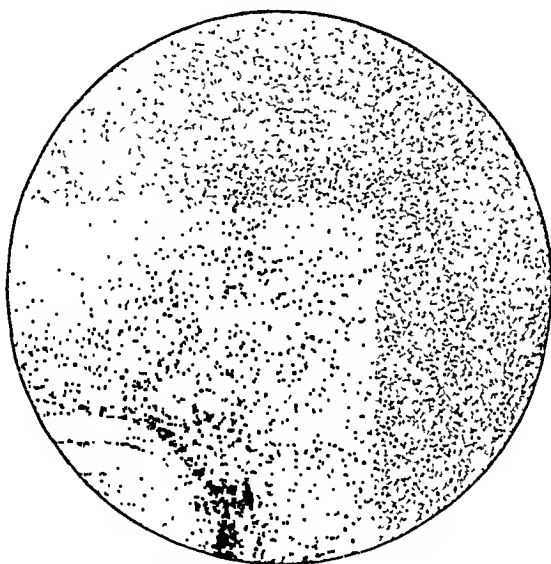
In the denser areas of the sclerosis, minute aggregations of atrophic cells are still visible, evidently the last remnant of gland structure.

Aggregations of small mononuclear round cells are also present resembling lymphoid tissue. Some of these round-cell accumulations, however, stand in immediate relation to bloodvessels, rendering it difficult to exclude a low-grade inflammatory process.

The large arteries passing into the gland while thickened, atheromatous, and containing calcareous plates are patulous throughout, as are also the larger vessels coursing within its substance.

*Adrenals.* The capsule of both suprarenal glands is thickened and infiltrated with round cells. The gland itself is the seat of extensive sclerotic, inflammatory and necrotic changes. Large areas of cheesy necrosis containing calcareous matter are surrounded by a dense sclerotic and inflammatory tissue containing numerous giant cells (Fig. 4).

FIG. 4.



Tuberculosis of adrenal. Round-cell infiltration. Giant cells and areas of cheesy necrosis. Hæmatoxylin and eosin.

Between and adjacent to these extensive areas of necrosis are islands of normal adrenal tissue. Approximately about one-fifth of the glandular structure of each suprarenal had been preserved. On the capsule of one of the glands is situated a small accessory suprarenal structure.

*Hypophysis Cerebri.* The hypophysis which to the naked eye appeared slightly enlarged, is quite normal in its histological appearances. No excess of the few globules of colloid-like material usually present in some of the acini is to be noted, and there are no evidences of glandular hypertrophy.

The bloodvessels and capillaries are distended with blood corpuscles.

*Kidneys.* Many of the glomeruli are sclerotic, and the capsules of others are thickened. There is some perivascular and peri-



glomerular sclerosis fading off into the surrounding renal tissue. The arteries show a considerable degree of arteriosclerosis. The renal epithelium, except in the immediate neighborhood of the sclerotic areas, is well preserved.

*Spleen.* Thickening of capsule and trabeculæ. Congestion and hemorrhages.

*Liver.* Moderate increase of the periportal connective tissue. Congestion.

*Heart Muscle.* No sclerosis and no fatty degeneration. Granules of yellow pigment arranged longitudinally within the muscle fibre near the nucleus (Brown atrophy).

*Pancreas.* The structure is normal.

*Skin.* Areas examined are normal.

*Tongue.* Normal.

*Examination of the Nervous System.* The brain, spinal cord, and the anterior crural, sciatic, pneumogastric and cervical sympathetic nerves were subjected to careful study by the usual laboratory methods (Nissl, Marchi, Weigert, hæmatoxylin, eosin, and Van Gieson). The result of this examination was entirely negative.

*Muscle.* The muscular tissue was normal save a necrosed and sclerotic area, probably due to arteriosclerosis with vascular occlusion. In this patch there was an increase of connective tissue, round-cell infiltration, atrophy, and degeneration of the muscle fibres. The muscle spindles and intermuscular nerve fibres were normal.

REMARKS. The important and essential change consists of an extensive atrophy and sclerosis of the thyroid gland. Even those vestiges of glandular substance still remaining are compressed or undergoing atrophy.

It is important to note that the hypophysis cerebri, which normally contains disks of a colloid-like material was not the seat of any considerable compensatory hypertrophy.

The slight enlargement noted seems to be sufficiently accounted for by congestion and the normal variation in the size of this organ.

The coexistence of a chronic tuberculosis of the adrenal glands must be regarded as a rare and curious example of a pathological coincidence.

I am unable to find any record in the literature of a similar combination of lesions.

In the tables of the Report of the London Clinical Society on Myxœdema,<sup>1</sup> case No. 42 showed a beginning tuberculosis of the suprarenal glands. In this case, however, the tubercular manifestations were general throughout the body. In my case the characteristic symptoms of Addison's disease (pigmentation of the skin and gastrointestinal disturbances) were absent. Evidently adrenal tissue still persisted in a sufficient quantity to carry on the function of the glands.

As asthenia is common to both diseases, it is impossible to deny that this symptom was not in part due to the suprarenal changes.

Myxœdema is characterized by two groups of symptoms, the one referable to the skin and its appendages, the other to the central nervous system.

The dermal changes so characteristic of the disease are associated with the deposit of an elastic, gelatinous substance in the subcutaneous tissue yielding chemically a large proportion of mucin (50 per cent.). Halliburton, Hun and Prudden<sup>2</sup>).

In some cases the connective tissue surrounding the hair follicles, sebaceous and sweat glands has shown various degrees of hyperplasia.

Those symptoms indicating derangement of the central nervous organs, quite as characteristic in their way, may be grouped as general, special, and mental symptoms.

As *general* may be mentioned headaches, vertigo, insomnia, convulsions, tremor, torpor, somnolence, asthenia, motor weakness and inco-ordination, paræsthenia, and diminished sensibility.

*Special.* Amblyopia, limitation of the visual fields, central color scotoma, temporal hemianopia, blindness, tinnitus aurium, and deafness. Subjective sensations of taste and smell.

*Mental.* Loss of memory, extreme sluggishness of thought and perception, delusions, hallucinations, melancholia, and mania.

While some of these nervous manifestations may be referred with justice to the involvement of the peripheral nerve endings in the swollen skin and mucous membranes, and some to pressure on the optic chiasm by an enlarged hypophysis cerebri, the greater number are of purely central origin.

It is singular that symptoms of such gravity and persisting for so long a time, often for years, should be unattended by permanent alterations of nerve structure. But such is the case.

It has been impossible to demonstrate in the central nervous system, uniform structural change which might serve as their basis.

Those described are so inconstant, variable, and uncertain in nature, that one hesitates incorporating them in the pathology of this affection, properly speaking.

Among the lesions hitherto described may be mentioned œdema, congestion, and hemorrhages of the cerebral cortex; vacuolation and degeneration of the nerve cells, similar to those described in epilepsy (Whitewell<sup>3</sup>); diffuse increase of the connective tissue of the large nerve trunks; atrophy of the cerebral cortex.

Savage<sup>4</sup> asserts that he has observed "changes in the brain and cord which would account for progressive weak-mindedness."

In other cases the central nervous system was entirely normal.

The nervous system in the classical cases of Hun and Prudden was entirely negative.

The Sub-committee of the Clinical Society of London in their report recognized no essential changes in the cerebrospinal or sympathetic nervous systems.

The present study confirms these negative results.

Many curious theories have been advanced in the past, in explanation of the origin and mechanism of production of the nervous manifestations of myxœdema.

Hadden<sup>5</sup> referred the condition to a contraction of all the peripheral lymphatics, due to a disturbance of centres seated probably in the medullar and acting through the sympathetic system; even the atrophic thyroid was regarded as of secondary origin.

Clouston<sup>6</sup> is responsible for the ingenious theory of a saturation of the neuroglia of the brain cortex in much the same manner that the subcutaneous tissue is affected, in this way interfering with the nutrition of nerve cells and the transmission of impulses.

Others ascribed the condition to the padding of the peripheral nerve endings by the myxœdematous deposit, thus interfering with the transmission of afferent impulses, the central structures suffering secondarily by virtue of the defective afferent conduction.

The toxic theory is that which finds most favor at the present day, but even here authorities differ as to the exact nature of the toxic substance in question.

While all concur that the symptoms are produced by an absence of the secretion of the thyroid gland, it is still one of the mooted questions of chemical pathology as to whether this secretion is itself essential to metabolism, or whether its beneficial influence consists in neutralizing products of metabolism otherwise possessing toxic properties (Ewald<sup>7</sup>).

The gradual reawakening under thyroid therapy, from this state of extreme mental and physical torpor, which Charcot so aptly likened to that of hibernation in animals; the disappearance of hallucinations and delusions and the eventual complete restoration of mental and bodily health after years of partial dementia, furnish strong clinical evidence that the nerve element in myxœdenia is not dependent upon organic changes in the neural structures of the body. If such are present they should rather be regarded as secondary in nature or ascribed to some other complicating factor.

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## A CASE OF MULTIPLE CEREBROSPINAL SCLEROSIS.

WITH REMARKS UPON THE PATHOGENESIS OF THE AFFECTION.

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THE consensus of opinion regarding the frequency of multiple sclerosis is that it is a rare affection in this country. This view is based upon the fact that typical cases presenting the classical symptoms are comparatively few. We should not, however, forget that in its early stages and in certain cases even in the latest stages the diagnosis of the affection is exceedingly difficult; perhaps, therefore, the disease is less frequently recognized than we would expect. Charcot had long ago pointed out the polymorphous character of this curious disease and the erroneous diagnosis made in many cases. Recently Hoffmann (*Deutsche Zeitschr. f. Nerv.*, 1902) has expressed the same view. Indeed, he maintains that the affection is one of the most common of organic nervous diseases. Being clinically often difficult of recognition, the thought arises whether the low percentage of cases in this country, as compared with Europe, may not in part be due to the small number of necropsies reported. In fact, as far as we know, only six cases with pathological findings have been reported in the United States: two by Spiller, two by Spiller and Camp, one by Burr and McCarthy, and one by Hunt. The following case is, therefore, the seventh:

L. C., female, aged twenty-nine years, white, entered the Philadelphia Hospital August 26, 1903, with the following history: Complaining of pain and tenderness in the pelvic region and profuse leucorrhœa. She was admitted to the gynecological wards. She had menstruated at twelve and had married at seventeen. She had never had living children, but three miscarriages. Three years previous to admission she fell and struck on the buttocks; since then the nervous disturbances enumerated below gradually developed. An operation showed cystic ovaries of long standing. Oöphorectomy was performed. Later she was transferred to the Nervous Wards, where the following symptoms were elicited. The body was much emaciated and distinct atrophy of individual groups of muscles, especially those of the thenar and hypothecar, were noted.

There was complete loss of power in the lower extremities. She could not flex or extend her legs. There was double foot-drop; the left foot was rotated inward. The knee-jerk was increased on both sides; ankle clonus existed on the right; Babinski was present on both sides. Examination for sensation showed a hyperalgesia of the whole body. The patient complained also of considerable pain in the joints, especially in those of the shoulders and hips.

There was a very coarse intention tremor, more marked on the right than on the left. The speech was distinctly scanning. Lateral nystagmus was present in both eyes. The pupils were unequal, the right larger than the left; they responded to accommodation, but very little, if any, to light. The left eye showed slight ptosis. Ophthalmoscopically the eyes were not examined. There was incontinence of feces and urine. A large bed-sore was present over the sacrum. Gradually the knee-jerks began to disappear; at first on one side, and then on the other. When shortly before death she developed a profuse diarrhœa, the knee-jerks were entirely gone. She died October 2, 1903.

The autopsy showed hypostatic congestion of the lungs, chronic parenchymatous nephritis, pyelonephritis, cystitis, and colitis. The brain was deeply injected; the pia-arachnoid slightly œdematous. Beneath the tentorium there was a large amount of clear, straw-colored fluid. The dura of the spinal cord was distended likewise with a straw-colored fluid.

#### MICROSCOPIC EXAMINATION OF THE BRAIN, CORD AND PERIPHERAL NERVES.

*Cord. Cervical Portion* (Weigert and Weigert-Pal methods). Transverse sections reveal great areas of sclerosis involving extensive destruction of the nervous tissue. From above downward the anterior cornua have gradually disappeared. In the upper levels the most anterior portions only are preserved, while in the lower cervical segments they are entirely absent. In the white substance the sclerotic areas also have entailed extensive destruction and some degeneration of fibres. In the upper segments the anterior white columns are intact, but as we descend to the thoracic portion they become gradually reduced. The lateral columns and the posterior columns of the cord, on the contrary, are almost entirely absent in the upper levels, but are preserved to some extent in the lower levels. A small band of healthy fibres is seen at the periphery of the cord surrounding the sclerotic areas. It is to be noted that healthy fibres are everywhere intermingled with the degenerated ones. The degeneration as well as the sclerotic areas are not symmetrical nor equal in extent in the two halves of the cord. The posterior roots show distinct degeneration at the level of their entrance into the cord, but only on one side. The anterior roots

also show some degeneration in the lower cervical portion. The bloodvessels around the cord show distinct dilation with thrombotic foci, and in some places present signs of endoarteritis and periarteritis. Marchi's method shows clearly very marked recent degeneration in areas which are apparently normal with Weigert's stain.

*Thoracic Region.* As in the cervical cord, there is extensive discoloration of the gray matter. In a small portion only of the thoracic cord are parts of the anterior cornua preserved; all the rest of the gray matter is destroyed. The anterior white columns, as in the cervical cord, are intact. The reduction of the anterolateral columns continues down the dorsal cord, so that we find only a very small area preserved on one side and extensive degeneration on the other. The posterolateral columns are totally destroyed with the exception of a few fibres in the direct cerebellar tract on one side and an extremely narrow peripheral band on the other. The posterior columns are entirely destroyed on one side, while on the other they are reduced to a few fibres. The posterior roots are destroyed on one side and much degenerated on the other. The bloodvessels are in the same condition as in the cervical region. Marchi's method shows recent degeneration in the pyramidal tract and in the posterior columns.

*Lumbar Cord.* There is complete destruction of the anterior portion of the anterior cornua. The anterior white columns and anterolateral ground bundle are destroyed in the upper portion, but only partly degenerated in the lower portion. The crossed pyramidal tracts show distinct degeneration through the entire lumbar segment. The posterior columns, as well as the roots, are normal. The bloodvessels are unusually dilated and thickened, especially in the lower portion. Marchi's method shows recent degeneration in the anterior columns only in the upper cervical segment.

The *sacral cord* shows almost complete absence of gray matter, and the white substance contains only degenerated fibres. The roots are intact. The bloodvessels show the same changes as in the other portions of the cord.

*Medulla.* In the lowest segment the nuclei of the columns of Goll and Burdach are totally destroyed; in the columns themselves there remain very few fibres; the rest are degenerated; the same condition is noted in the decussating fibres. At the level of the beginning sensory decussation there is seen the same destruction of the nuclei gracilis and cuneatus, areas of degeneration in the posterior columns, and a marked sclerotic area in the sensory decussation. In sections above we see reappearance of a great many fibres in Goll's and Burdach's columns, but intermingled with a great many degenerated fibres, more upon one side than upon the other. The above-mentioned nuclei, also Monakow's nucleus are entirely absent. The destruction of the sensory decussation extends forward, but unequally, into the pyramids, and involve also a large

part of the nucleus of the hypoglossus. Very few cells are seen in the nuclei of the eleventh and twelfth nerves. In upper sections we see the sclerotic process involving also the gelatinous substance of Rolando, the fasciculus solitarius, the nuclei of the eleventh and twelfth nerves, the interolivary portion of the formatio reticularis alba and portions of the pyramids. These changes are not symmetrical.

In sections above, the nuclei of Goll and Burdach reappear again, but unequally, on both sides; the sclerotic process is seen to extend to the restiform bodies. Gradually in sections higher up the

FIG. 1.



Besides other sclerotic areas, degeneration of the optic tracts and partly of their chiasma are to be noted. Also the crura are involved.

nuclei and the columns of Goll and Burdach become more and more free from the sclerotic process and show only degeneration. The latter process involves also the cerebello-olivary fibres which surround the descending root of the fifth nerve. The pyramids also show only degenerated areas. In the sections following, the nuclei of the eighth, ninth, and tenth nerves also reveal partial destruction. Higher up we see also that the tuberculous acusticus, the two nuclei of the eighth, the solitary bundle, the olives with their afferent and efferent fibres, are more or less and unequally on either side involved; the pyramids always show areas of degeneration. The posterior longitudinal bundle, the median fillet, the trapezoid body, and the

inferior cerebellar peduncles are also partly destroyed. Similar conditions are noted in the knee of the seventh, in the nucleus of the sixth, in the descending sensory root of the fifth; also in the posterior transverse fibres of the pons and in the pyramidal bundles. At the level of the cerebellum we see that the three cerebellar peduncles, both roots of the fifth nerve, the middle lobe of the cerebellum, besides the pyramidal bundle—all suffer considerably. At the level of the aqueduct of Sylvius, the pathetic nerve is almost entirely destroyed on one side. In the subthalamic region one red nucleus and one posterior longitudinal bundle are more or less degenerated. The optic tract in front of the mammillary tubercles is totally degenerated on one side and slightly on the other. The

FIG. 2.



Plaques of sclerosis, particularly in internal capsule and crura.

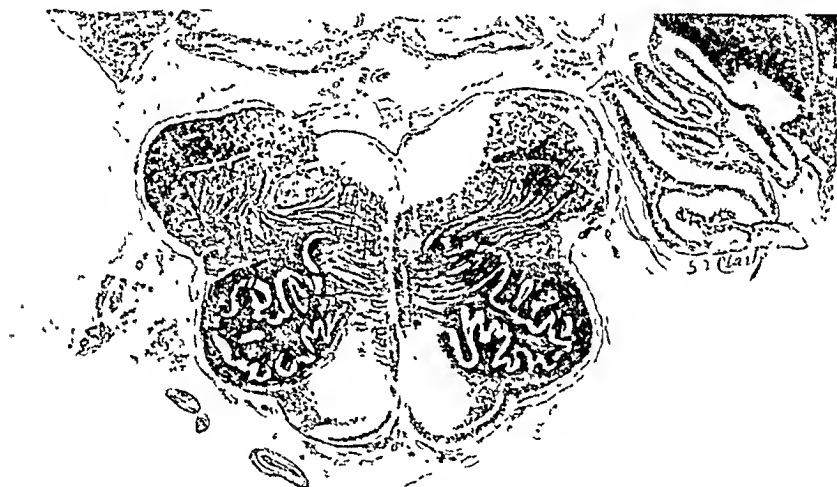
foot of one cerebral peduncle is markedly degenerated in its inner third and the other in its middle third. A vertical section through the posterior limb of the internal capsule, at the level of the posterior commissure and the pineal body, shows an area of degeneration in the middle of the internal capsule; the degeneration involves also the fibres passing from the optic thalamus to the capsule and the posterior commissure itself. The degeneration is also seen to involve the fibres going from the thalamus to the cortex. Areas of degeneration are found besides in the white matter of the motor area of the brain and in the cerebellum. The bloodvessels of the medulla show the same change as in the cord.

A review of the pathological findings show that the condition of the gray matter is as follows: In the sacral portion of the cord



it is totally absent, in the lumbar cord it is preserved, and again begins to disappear in the thoracic and cervical segments. As to the white substance, it is preserved to a great extent in the lower cord, but in the thoracic segments, while it presents areas of degeneration, it contains also vast areas of total destruction, irregularly distributed. The height of the destruction is reached in the cervical cord. In taking up the individual tracts of the cord, we see that the anterior and the anterolateral columns are gradually reduced from above downward. No such regularity could be traced in the posterior and posterolateral columns. The irregularity of the sclerotic process is particularly marked in the medulla; while in one section the areas of destruction are multiple and extensive, in others there is merely a marked diminution. However, we can say that the gray matter—viz., the nuclei—suffers more than the

FIG. 3.



Sclerotic areas in the pyramids and restiform bodies.

fibres. Almost all of the nuclei of the cranial nerves and the nuclei of the medulla and pons are affected. The motor as well as the sensory decussation, various afferent and efferent fibres of the olives, the three pairs of cerebellar peduncles, the pyramidal bundles, the middle lobe of the cerebellum and the hemispheres of the latter, the geniculate bodies, the red nuclei, the posterior longitudinal bundles, the internal capsule, the thalamic fibres going to the internal capsules and to the cortex, finally the optic tracts—these are the structures affected by this curious disease process. The characteristic feature consists in the remarkable irregularity of the distribution; the site and extent of the pathological areas vary from section to section, and there is no symmetrical arrangement of the patches in the two halves of the sections. Marchi's method always showed recent degenerations among the preserved fibres. The

bloodvessels showed, all along the cerebrospinal axis, distinct and in some places marked dilatation and thickening of their walls. Leukocytic infiltration of the walls of the bloodvessels and thickening of the meninges with nuclear infiltration are seen at the periphery and in the fissures of the cord.

The condition of the cells and of the axis cylinders deserve special mention. In contrast with the extensive foci of sclerosis in which the fibres of the white matter are entirely destroyed, we found, curiously enough, marked preservation of a large number of cells; even in the midst of an entirely discolored portion, showing total destruction of tissue. Thionin stain revealed some cells intact. It is true that in similar areas the majority of cells are absent, but it is certainly surprising to find normal cells in foci of such a character. A quite considerable number of normal cells are seen in

FIG. 4.



Anterior and lateral columns show areas of sclerosis. Secondary degeneration.

areas where the nervous tissue, if not entirely, is at least to a great extent damaged. A glance at these findings gives the impression that the destructive process had originally no predilection for the cells, which it, as it were, avoided and affected only the white substance. There are, however, some degenerated cells in which are to be seen the usual chromatolysis, with displacement of the nuclei and deformities of the entire cell.

Similar remarks can be made about the axis cylinder. Not only among the ordinary degenerated fibres, but also in the completely destroyed areas, axis cylinders are seen to be present. Naked axis cylinders are found scattered in the most diseased areas. Transverse sections, however, show that they are irregular in form, angular, large, or unusually small (atrophy). That they are diseased there cannot be any doubt, but the fact that they are present, without their medullary sheaths, even in dense islets and sometimes

normal in shape and size, is strongly suggestive of the view that the sclerotic process has a tendency to affect primarily the medullary sheaths and spare for a long time the axis cylinders.

The pathogenesis of disseminated sclerosis is still a subject of discussion. According to the vascular theory, the destruction of nerve tissue is secondary to a primary alteration of the vessel walls. Although in a number of cases endarteritis and periarteritis have been found in multiple sclerosis, some competent investigators have failed to find such lesions, or, at least, changes that are characteristic and pronounced. Our case presents dilatation and thickening with leukocytic infiltration of the vessel walls, but these changes are not equally nor extensively distributed. Moreover, in certain regions, in which the destruction of nerve tissue is the least marked, the vessel changes are the most pronounced, as, for example, in the lumbar segments of the cord. In other words, the degenerated condition of the vessels is not in keeping with the destructive process in the nerve tissue. It is very probable that these changes do not bear to each other the relation of cause and effect. Further, it is not impossible that the same pathogenic agent (whatever it may be) affects both tissues, nervous and vascular, at the same time, though in varying degree. Eduard Mueller, who has recently made multiple cerebrospinal sclerosis the subject of an exhaustive treatise, goes so far as to regard the vascular involvement as secondary to the involvement of other tissues.

Regarding the lesions themselves, it is noteworthy that the nervous elements proper—that is, the axis cylinders and the nerve cells—suffer last and least. All observers agree in the frequency with which nerve cells and axis cylinders are found intact in the sclerosed areas. The myelin disappears long before the axis cylinder is destroyed. This doubtless accounts for the infrequency and merely occasional presence of secondary degeneration. Whatever the origin of the disease really is, it is not impossible that we have to deal here with a sclerosis of the neuroglial tissue. This position is strongly advocated by Mueller. In confirmation of this view, Mueller points to an instance observed by him in which multiple sclerosis and syringomyelia coexisted in the same patient. He would, indeed, regard multiple cerebrospinal sclerosis as a multiple gliosis of the nervous system. However, the rarity of the concurrence of syringomyelia and multiple sclerosis would alone throw doubt upon this interpretation. Furthermore, gliomatous lesions of the nervous system observed elsewhere than in the cord are not in any sense comparable to typical plaques of sclerosis. Again, there are many facts which render a theory that this disease is dependent upon some abnormality of tissue development, embryonal or otherwise, untenable. That the lesion may have its origin in the glia is not impossible. However, all that we have a right to infer is that neither the nerve cells nor axis cylinders,

on the one hand, nor the bloodvessels, on the other, are primarily involved.

An interesting pathological feature of our case is found in the presence of secondary degeneration, which, as is well known, is a rare occurrence in multiple sclerosis. Beginning in the motor area and continuing through the internal capsule down to the medulla and the very lowest portion of the cord, we found in the pyramidal tract, besides isolated sclerotic islets, also degenerated fibres intermingled with normal ones. We are, however, unable to say whether this secondary degeneration is an independent condition or is in relation with the sclerotic foci.

Finally, we wish to call attention to an interesting phenomenon observed during the patient's life, and which was of some diagnostic importance—viz., the condition of the knee-jerks. While at first they were exaggerated and remained as such for a long time, they gradually diminished in intensity and finally disappeared. This was an indication of an extension of the pathological process from the white matter to the gray. We consider this observation noteworthy, as some competent authors (Marie and others) believe that the knee-jerks are never absent in disseminated sclerosis. As a last interesting feature of the case we wish to emphasize the involvement of the third, fourth, and sixth nerves, with their nuclei, and also the optic tracts.

## A CASE OF INFECTIVE, LATERAL, SIGMOID, SUPERIOR PETROSAL SINUS AND JUGULAR THROMBOSIS; OPERATION; RECOVERY.<sup>1</sup>

BY JOHN D. RICHARDS, M.D.,  
OF NEW YORK.

THE case is one in which the infective thrombosis was of otitic origin, in which the clot extended from the torcular Herophili to the junction of the internal jugular and facial veins, and in which there was prior to the operation neither chill, remitting temperature, nor sweat. A beginning papillitis in the opposite eye was the chief sign pointing to intracranial involvement, together with the mastoid symptoms.

The history is that four years ago the same ear was involved in an acute middle-ear suppuration, the duration of which was a week or ten days, with apparent complete recovery. The accuracy of this statement I doubt, as at the time of the present operation the patient had a condition which appeared to be that of a chronic suppurating

<sup>1</sup> Presented at the New York Academy of Medicine, May 12, 1901.

ear. Ten months ago he had a repetition of his former trouble; there was earache, followed in two days by profuse purulent discharge, which gradually diminished until the end of the third week, when it apparently ceased. Two days after this apparent cessation, spontaneous pain was referred to the mastoid region of the involved side, and intermittent headache was complained of. No fever was noticed by the patient or detected by his physician, and he was up and about; on one occasion he vomited. The membrana tympani was lustreless, but not reddened; a small perforation occupied a point in the posteroinferior quadrant midway between the umbo and the periphery, and there was scarcely enough non-fetid pus present in the canal to moisten the cotton applicator; for several days the ear had been irrigated. There was no sagging of the posterosuperior portion of the membranous canal, nor any bulging of the posterosuperior sector of the drum membrane. Upon firm pressure over the mastoid antrum, tenderness was moderate, over the tip marked, over the premastoid lamina exquisite. In the emissary vein region there was neither tenderness nor oedema, and the upper portion of the posterior cervical triangle was negative.

The temperature at this time was 99°, with pulse and respiration in accordance. The fundus of each eye was normal; there was no tenderness over the upper third of the jugular vein, nor any noticeable enlargement of the cervical glands. An operation was advised and was performed on the following day. During this interval there was no rise of temperature. Upon removing a thin mastoid cortex, pale velvety granulations, as yet not broken down and seemingly under considerable pressure, pouted into the wound. The mastoid was pneumatic throughout, and the manner of distribution of the diseased areas, they being sandwiched in between clusters of perfectly healthy cells containing a straw-colored fluid, strongly suggested the method and route of infection as a septic phlebitis of the minute veins, contiguity and gravity apparently having influenced but little the manner of the spread.

A Schwartze-Stacke operation was performed. There was no macroscopic pus present in either the mastoid cells, the antrum, or the tympanic cavity, but more or less profuse exuberant granulations. The disease had exposed about one-half inch of the middle of the vertical limb of the sigmoid sinus by erosion of the overlying groove, and here the vessel wall was covered by dirty blackish, breaking-down granulations in contact with a similar mass occupying the mastoid cells immediately anterior.

In order to get healthy dura exposed on all sides and to remove the diseased bone, it was necessary to remove the overlying sinus groove from a point slightly beyond the knee on the torcular side to a point near the jugular bulb; also the bone anterior to the total anterior border of the descending sinus limb for half an inch, and posteriorly it was necessary to make a second perpendicular incision

to the original curvilinear incision, peel back a hand-shaped flap, and remove a considerable portion of the occipital bone, thereby exposing the anterolateral aspect of the cerebellar dura. A third posterior incision was made extending upward and backward to the parietal bone, and a portion of that structure was rongeured away. There was present an extensive osteomyelitis. Upon palpating the sinus it was impossible to differentiate between sinus and brain pulsation, and the impression given me was that I was dealing with a sinus the external wall of which was merely covered by granulations. The expression experiment was tried, but gave no information, and in view of the fact that the temperature had at no time been above  $+99^{\circ}$ , that there were no definite symptoms pointing to thrombosis, and realizing the uncertainty of palpation as a factor in the diagnosis of this malady, it was decided to return the patient to bed. Three hours later the temperature had risen to  $100.4^{\circ}$ , and continued thereabouts with slight fluctuations of less than one degree until the following day, when I again visited him. At this time, upon the malar region of the involved side, there was a blush such as is not uncommonly seen in lobar pneumonia. The respiration and pulse were not accelerated, and a careful examination of the thorax, with the exception of a few fine scattered rales, proved negative. The fundus of each eye was again examined; the left papilla remained unchanged from its previous appearance; the right had, however, undergone a degree of blurring which was unmistakably that of a beginning papillitis, and I interpreted it as a distinct march in the course of the symptoms, and decided to immediately investigate the sinus. The jugular vein was at no time tender to the touch, and no induration could be detected over its course. The sinus was opened immediately below the knee, and no bleeding occurred; its lumen was occupied by a firm, granular clot. One blade of the scissors was then introduced within the lumen of the vessel and its external wall slit up beyond the knee and out on the lateral sinus to the limit of bone removed, with the result that no flow occurred.

At this time it became evident that the case was an extensive one, and I turned my attention to what I considered the most important factor, the lower end of the sigmoid sinus. The external wall of the vessel was next slit down to a point as near the jugular bulb as possible, but no bleeding occurred. Believing it to be under these conditions an unjustifiable procedure to curette in the region of the bulb for the purpose of getting a return flow from below, a jugular resection was proceeded with. Upon exposing this vessel in the neck, the reverse blood tide was seen to extend only to the point of entrance of the facial into the jugular vein. Above this point the vessel was occupied by a fairly firm clot; below it was only partly filled and with each inspiration collapsed, during which time the limit of the thrombus was distinctly marked.

The vein was ligated at a point behind the sternoclavicular joint, and together with portions of its branches was resected. Its upper end was not ligated, as the vessel was thrombosed. The neck wound was later packed and treated as an open wound, no sutures being taken. Attention was next turned to the sigmoid sinus, and with a curette the clot in the region of the bulb, as well as could be, was removed and a thin strip of gauze introduced within the lumen of the vessel and carried down to the bulb for drainage. The clot occupying the descending limb of the sinus was next removed, the external wall of the vessel cut away, and, upon reaching the region of the sinus knee, it was seen that the superior petrosal sinus was occluded. This vessel was explored inward and opened to a point opposite the posterior semicircular canal.

A return flow from this source was never obtained. An incision was next made out to the torcular, the scalp retracted, and a canal in the skull corresponding to the external wall of the lateral sinus was made. The external wall of the sinus was slit out to a point about three-quarters of an inch from the torcular, and midway between this point and the sinus knee four or five drops of fluid, reddish-yellow pus exuded from the clot. It was the only point at which the thrombus had broken down, and this was evidently the pathological explanation for the absence of clinical symptoms. The pus products, being blocked from the general circulation on either side by firm clots, were practically extraneous to the system. Not considering it a safe procedure to pass any instrument into the torcular for fear of dislodging the distal end of the thrombus and having it returned as septic emboli through the opposite side into the general circulation, I was preparing to explore the torcular and its confluent sinuses, when it occurred to me to block the opposite jugular for the purpose of creating a reverse pressure upon the torcular end of the thrombus, with the hope of dislodging it. This was done, and immediately there followed a slight spurt of blood, a sudden stoppage of the stream, again a spurt of blood, and the extrusion of a thin, small, squeezed-out, liver-colored clot, about one-half an inch in length. This evidently represented the axis of the extreme torcular end of the clot, it being less firm and less resistant to pressure than the more peripheral portions, gave way, and a mere tunnelling resulted.

This was the explanation which at the time I held accountable for the slight and scarcely satisfactory bleeding from the torcular, and it seemed most probable that the adjacent sinuses were not involved, otherwise they scarcely would have sustained a blood column through which such a degree of pressure as was necessary to dislodge the clot could have been transmitted.

Before terminating the operation a curette was introduced into the extreme torcular end of the sinus and gentle curetting was done, the precaution being taken to first have the assistant exert pressure in the neck over the course of the opposite internal jugular, primarily

for the purpose of cutting off the aspiratory influence of inspiration, secondarily for aiding in a backward flow. On the fourth day after the operation papillitis appeared in the left eye, and later reached in both the elevation of about  $\frac{1}{3}$  mm., the vision remaining normal throughout, and no atrophy ensuing. On the fifth day the dressing was changed, and when removing the packing from the neck several drops of pus exuded from the upper wound. The pus in the lateral sinus contained pure staphylococci; unfortunately the torcular end of the clot was lost; it was in all probability non-infective. The clot occupying the upper portion of the jugular vein was negative. Staphylococci were present in large numbers in the wall of the jugular vein, and had invaded that structure to a point considerably farther down toward its cardiac side than the macroscopic appearance had indicated.

I think this shows conclusively that the naked-eye line of demarcation between involved and uninvolved vessel wall is not always an index of the extent to which the vessel suffers bacterial invasion, and that, therefore, when it becomes necessary to resect the internal jugular in such cases, ligation should be at a point low down; otherwise operative interference may not intercept the invading process, a portion of infected vessel may remain, calling for a reoperation through the continuance of symptoms, and possibly eventuating in a fatal issue.

The ear cavity was secondarily skin-grafted, with the exception of the region of the round and oval windows, a precaution which I consider advisable, as the resulting epidermitization, according to the natural process, blankets less effectually, I believe, the sound waves than the comparatively thick layer of membrane artificially placed in the process of grafting.

The practice of exerting pressure in the neck (low down) over the course of the internal jugular vein while attempting to remove a thrombus from either the torcular end of the lateral sinus or from the region of the bulb, for the purpose of preventing emboli passing into the general circulation, is a procedure which I have never before seen used.

Any instrumentation in the lower portion of the sigmoid sinus, as in the attempt to curette a thrombus from the region of the bulb, is liable to loosen emboli which may pass into the general system by aspiration. By exerting firm pressure over the jugular vein of the same side during our manipulation, we accomplish to some extent the elimination of the aspiratory influence, and, in addition, materially aid in flushing the suspended particles backward through the sinus wound. A very valid objection to the practice lies in the probability of septic particles being forced not only backward through the opened sigmoid sinus, which would naturally be the path of least resistance, but also through the inferior petrosal and the smaller veins over to the opposite circulation. This objection is,



however, slight as compared to the great probability of emboli passing through the internal jugular of the same side by aspirating when this vessel is uncompressed. It becomes a question of choosing the lesser of two evils. Since the present case was operated, on several occasions I have had, while operating upon infective sinus and jugular cases, the opportunity to observe more carefully the effect of the above procedure, and to somewhat modify it. When attempting to curette a thrombus from the region of the bulb, pressure should be made not only over the internal jugular of the corresponding side, but over both internal jugulars. By doing this the backward pressure is noticeably increased, and, in addition, the opposite internal jugular to the side of operation should be compressed, either simultaneously with or slightly prior to the jugular of the operated side. By compressing both vessels, the aspiratory influence of inspiration is more effectually eliminated. By compressing the opposite vein immediately prior to its fellow, the venous system of that side becomes primarily congested, and consequently emboli would not so readily be forced through the communicating veins to the opposite circulation. The reverse proposition is likewise to be considered, but I believe pressure over both vessels to be of decided advantage. I do not advocate, however, the attempt to curette the region of the jugular bulb, prior to jugular ligation, after having slit the external wall of the vessel down to a point as near the bulb as possible, and having failed to get a spontaneous return flow from below. To those who insist that this practice is conservative, I believe the above procedure will be of advantage and will lessen the probability of general sepsis.

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## POSTERIOR-BASIC MENINGITIS.

BY HENRY KOPLIK, M.D.,

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THIS peculiar form of meningitis was first brought prominently to the notice of the profession by Gee and Barlow, who, in the *St. Bartholomew Reports* of 1878, described twenty-five cases of meningitis occurring in infants below two years of age. Some of these cases had existed from birth and others occurred sporadically at varying periods. The essential feature of all the cases described was, in the words of the authors, "the holding back of the head." In fact, they called this form of meningitis "cervical opisthotonos of infants," and laid special stress on the holding back of the head as the essential symptom of the disease. They also accentuated the fact that in tuberculous meningitis and other diseases the holding

back of the head was an occasional occurrence, whereas in this form of meningitis it was a constant, unvarying symptom.

In some of their cases the onset had been gradual and in others sudden. In those cases in which the onset had been sudden the opisthotonos alone, or accompanied by fever, vomiting, rigidity of the limbs, and convulsions, seemed to be characteristic. The associated symptoms in their cases included rigidity of the limbs and convulsions throughout the course of the disease. The course of the disease in all these cases was chronic and only three of their twenty-five recovered. The duration of the disease, from its onset to the fatal termination, varied from twenty-seven days to nineteen months.

Post-mortem examination, in all cases in which it could be obtained, revealed the fact that no tubercle existed either in the brain or other organs of the body. There was lymph in varying quantities at the base of the brain, and the ventricles were dilated in most cases. In some cases there was otitis, but the other viscera showed no changes.

As to the etiology, these authors, at the time this paper was written, considered syphilis as a doubtful factor, and ventured the opinion that some of the acute cases with sudden onset resembled "epidemic cerebrospinal meningitis" of the sporadic variety.

In 1897 Carr described a number of cases of hydrocephalus with dilatation of the ventricles of the brain following meningitis, and ventured a theory, to which we will return, as to the cause of hydrocephalus in these cases. His cases resembled essentially those of Gee and Barlow.

In 1898, Still again called attention to this affection in an article in the *Journal of Pathology and Bacteriology* of that year. He mentioned the cases of Gee and Barlow, also stated that the disease occurs sporadically, and is uncommon in England and America, only forty-nine cases having presented themselves during the previous ten years in the Hospital for Sick Children in London. In this article he describes the findings in eight of the cases. He investigated post-mortem the exudate found in the ventricles and in the sub-arachnoid space, and isolated from these exudates a diplococcus which closely resembled the diplococcus intracellularis of Weichselbaum. He thought, however, that it grew more luxuriantly in broth and on agar-agar and glycerin-agar. He failed to find it in some of the chronic cases which had lasted several weeks, and he found it in the tendon sheaths in complicating arthritis in one case.

In describing the disease Still, in this article, considers it as not occurring in epidemics, but rather sporadically, and draws the distinction between epidemic cerebrospinal meningitis and these sporadic cases. In the cases he examined during life herpes and rash were absent. There were some minor differences also between these cases and the epidemic form of cerebrospinal meningitis.

Still laid particular emphasis on the fact that cerebrospinal meningitis of the epidemic type was more rapidly fatal than the posterior-basic meningitis, but that they resembled each other in that they both seemed to affect, by predilection, the base of the brain. He concludes that posterior-basic meningitis is a disease of infancy of a non-tuberculous nature, due to a specific micro-organism, and that this micro-organism is almost identical with the diplococcus of Weichselbaum and Jäger. In other words, he did not think that this disease which we are describing could occur in epidemics. The periarthrits which complicated one of his cases was due to the essential cause—the diplococcus intracellularis.

In another article by Still in the *British Medical Journal*, 1898, he further describes the clinical features of these cases. Most of them occurred within the first two years, rarely after the second year of life, and he laid stress on the fact that many of these cases, in London, at least, have been reported as cases of tuberculous meningitis—an experience which the author has had in New York.

Still divides these cases distinctly into those which are fatal within six weeks, those which die after three or four months with hydrocephalus, and finally those which recover. In those cases which are fatal within six weeks post-mortem examination reveals lymph at the base of the brain and cord. In those which die after three or four months with hydrocephalus there is simply a thickening of the pia mater and arachnoid at the base of the brain, some adhesions between the cerebellum and medulla, and slight thickenings on the surface of the temporal or temporosphenoidal lobes. In the ordinary “suppurative vertical meningitis,” as he calls it, there are complications elsewhere. In this form rarely so. In fifteen cases of suppurative meningitis there were as complications empyema, pleurisy, pneumonia, ulcerative endocarditis, membranous colitis, necrosis of the petrous portion of the temporal bone, and erysipelas. In two cases of fifteen of basic meningitis there was inflammation of the tendon sheaths, and in one there was an accidental tuberculous focus in some of the viscera. In some of the basic cases there was a mucopurulent secretion in the middle ear, but in none of them was there evidence of mastoid disease or of extension of the ear disease to the brain or meninges.

Still, in this article, laid stress on the bacteriological findings as described in his paper in the *Journal of Pathology and Bacteriology*, and again reiterates the fact that the tuberculous foci found by him in some cases of this disease had absolutely no connection with the primary affection.

In an article on posterior-basic meningitis in Allbutt's *System of Medicine*, Barlow and Lees defined more clearly the pathological changes found in these cases. The inflammation begins at the posterior part of the base of the brain, in most cases, as the primary seat of inflammation, namely, the region where the brain and spinal

cord meet and where the cerebellum overlaps the medulla. From this site the inflammation spreads down the cord to a varying degree, upward along the line of the ventricles, and forward along the base as far as the optic commissure and tips of the temporo-sphenoidal lobes; or the inflammation may begin in the transverse fissure and choroid plexuses. At an early stage of the disease the products of inflammation, though circumscribed, may be suppurative, but later on they may become absorbed and opacities of the meninges with adhesions result. These adhesions may unite the medulla and cerebellum, obliterate the foramen of Magendie and the fourth ventricle. This gives rise to an accumulation of fluid in the ventricles and consequent hydrocephalus. In some of these cases the ventricular fluid is clear and in others it contains flakes of fibrin and pus. In the latter the ependyma is thickened. In some cases the viscera were normal, in others the lungs were collapsed.

In the Cavendish lectures of Osler this author describes a case of posterior-basic meningitis occurring in an older child, considers the etiology and morbid anatomy, but ventures no definite opinion as to the identity or classification of these cases, at the same time noting the work of Still and Gee and Barlow.

The author of this paper has seen a number of cases of posterior-basic meningitis occurring sporadically throughout five years of continuous hospital service. He has never been able to establish, however, until recently the fact, which was doubted by Still, that these cases may occur in epidemics of cerebrospinal meningitis. In the recent epidemic of 1904 the author saw thirty cases of cerebrospinal meningitis in his hospital service. Eight of these were typical cases of posterior-basic meningitis, admitted at various periods of the affection. Some of these cases were as young as four months of age; most of them were below two years of age.

Of the eight cases of posterior-basic meningitis admitted to my service during the recent epidemic of cerebrospinal meningitis the ages ranged from four months to five years. They were, respectively, two infants of four months, one of six months, one of nine months, one child of two years, one of three years, and one of five years. Most of these cases thus were below two years of age. The symptomatology of those above this age varied somewhat from these children and will be regarded in a separate rubric to which we will return later.

The previous history was negative in all of the cases. In other words, there was no history in any case of syphilis or tuberculosis, either in the child or in members of the family. In one case there was a history of ear trouble dating two months before admission and lasting for two weeks, but this had no connection with the illness. In another case the child had had measles three months before admission and scarlet fever a year before this. These

diseases also had no connection with the illness for which the child was admitted.

As to the family history, it has been mentioned that there was no history of tuberculosis or syphilis or anything suggesting the disease in the child, father, mother, or other members of the family. In one case there was a history of miscarriage and of one child of the family having died of meningitis some years before the advent of the present case.

The duration of the disease before admission to the hospital varied in all the cases. One case was admitted the third day after the onset of the disease. This was the case of the child five years of age in which post-mortem examination revealed a form of posterior-basic meningitis, to which we will return. The other cases were admitted seven days, seventeen days, twenty-four days, four weeks, five weeks, and ten weeks after the onset of the initial symptoms.

The mode of onset, speaking now only of the cases below two years of age, which correspond accurately to those described by Gee, Barlow, and Still, in only one case was gradual; in all the others it was sudden. The child was taken with fever and vomiting, then it was noticed that there was rigidity of the neck, and in some cases convulsions occurred. These convulsions were repeated in one case daily for two weeks, the child being quiet in the interval of the convulsions. In other cases after the initial fever and vomiting the child became stupid; then the mother noticed that the fever continued or that the child became blind—in other words, did not notice or see things about it. Nourishment was taken by most cases at the time of the onset, unless rejected by vomiting. In the case in which the onset was gradual there is reason to suspect incorrect observation on the part of the mother, so that it may be said that in all cases the onset was sudden. In all cases the fever and vomiting were followed by rigidity of the neck, in some cases by convulsions, these symptoms being supplemented eventually by the so-called cervical opisthotonos.

When fully developed the picture of the disease as presented to us in the hospital was as follows: The children were emaciated; they lay quiet, seldom crying out; the head was retracted, there was marked or slight opisthotonos, the upper and lower extremities were adducted, the forearm being flexed on the arm, the thighs flexed on the abdomen, and the wrists and fingers flexed. In some cases the children presented the picture in the upper extremities seen in tetany, the so-called driving position of the hands. In other cases the lower extremities were extended and could not be bent, although the upper extremities would be strongly flexed. In the extended position of the lower extremities the thighs could not be flexed, nor could the lower extremity be flexed at the knee. The foot was strongly extended on the leg and the toes flexed into the plantar

surface of the foot, resembling the tetany position. Sometimes the body would be curved to an extreme degree backward, the head assuming an angle of almost 90 degrees with the spinal cord. At times this opisthotonos and tetanus would relax and the spastic phenomenon would not be so apparent. As soon as disturbed, however, or if the back were rubbed, the patients assumed again a position of extreme opisthotonos. In other cases, in addition to the picture thus presented, there was a tendency to cross the legs; in others there were purposeless movements of the upper extremities in a sort of arc in front of the face. The fontanelles, if still open, were bulging and the sutures, in some cases in which hydrocephalus had supervened, were pressed apart by the accumulating fluid in the ventricles. In one case spasmodic contraction of the muscles of respiration occurred at intervals to such an extent as to cause a peculiar hissing sound in the larynx and also an extreme bulging anteriorly of the thorax. In some cases there was strabismus; in other cases this was absent. There was no pulsation to the bulging fontanelle above described. As a rule, the lungs, heart, liver, and spleen presented nothing positive. In all cases the emaciation was so extreme that the abdomen was retracted or rigid.

Some of the children presented, as an accidental find, marked rachitis and cranial tabes.

The temperature, in those cases which had lasted for some length of time, would not range above the normal until close to the final issue. In other words, they ran a temperature simulating what is seen in tuberculous meningitis. One case, in the hospital for five weeks, had a normal temperature for three weeks after admission and then presented wide excursions of temperature, as high as  $106\frac{3}{4}^{\circ}$ , especially after lumbar puncture. These temperatures did not seem to be anything but cerebral temperatures, for lumbar puncture in the case just mentioned revealed nothing but sterile fluid. In another case, in which the post-mortem confirmed the diagnosis of posterior-basic meningitis, the range of temperature for fifteen days was normal with the exception of one day, when it rose to  $102^{\circ}$ . In one case, which does not belong to the rubric described by Gee and Barlow and Still, inasmuch as the child was three years of age, the patient died after twenty-four weeks of illness, and only during the first four weeks of the sojourn in the hospital was there any temperature. During these four weeks it ranged as high as  $105\frac{3}{4}^{\circ}$ ; during the remaining twenty weeks the temperature did not rise above the normal. In this case the child was admitted to the hospital on the seventh day of the disease, making a duration of twenty-five weeks.

Of the other symptoms of interest in these cases is, first, the condition of the fundus of the eye. In most of the cases below two years of age there was no change in the fundus; in other words, there was no optic neuritis, contrary to what is true of cases of

tuberculous meningitis, in which, in the majority of cases, there are changes in the fundus. In all of the cases of the Still type there were other signs which are generally included in the symptomatology of meningitis, such as *tâche cérébrale*, with evanescent erythemas due to vasomotor paresis. Kernig's sign in these cases is of very little value for two reasons: first, that these infants or children lie in a spastic or flexed position, and second, that in children below two years of age the presence or absence of Kernig's sign is a very difficult matter to substantiate. As to the Babinski reflex, in most cases it was absent; in others it might have been established in the course of the disease.

The leukocyte count in most of these cases is of great interest. In one case the leukocytes ranged from 14,000 to 17,000 to the cubic millimetre. In another case the leukocytes ranged from 10,000 to 30,000, the latter being the count at the close of the disease. In another case the leukocyte count was 19,000, the child dying three days after admission. In the case of an infant twelve months of age who was admitted on the twenty-fourth day of the disease the leukocyte count on admission was 26,000. It can thus be seen from this simple enumeration of the leukocyte counts that they were, as a rule, low, similar to what is seen in tuberculous meningitis, and therefore of no diagnostic value.

Of especial interest are the results of lumbar puncture. Our experience has been that lumbar puncture in posterior-basic meningitis is not always successful in evacuating fluid. In some of our cases we have proved that the cause of the so-called dry tap on lumbar puncture is due to the closing up of the canal of Magendie by exudate, and also the matting together of the spinal canal in the vicinity of the cerebellum and pons to such an extent that the subarachnoid fluid cannot flow from the subarachnoid space and ventricles of the brain into the space of the cord and out, and thus through the cannula in the lumbar region. In cases in which hydrocephalus had supervened and in which the disease had lasted for weeks, lumbar puncture was of only negative value so far as diagnosis was concerned, inasmuch as repeated puncture in such cases revealed a sterile fluid. Although the fluid in some cases was not quite clear, no micro-organisms were found either by spread or culture. This must be explained by the fact that in these cases the micro-organisms have really died out, and the few that remained were found only post-mortem, as in one case, in the ventricles of the brain.

Of the six cases below two years of age, which correspond absolutely to those described by Still, one gave a negative result by lumbar puncture, that is, only a few drops of fluid being obtained during life. In this case post-mortem examination of the fluid of the ventricles revealed the meningococcus. In another case, four months of age, although typical of the disease which we are describ-

ing, the lumbar puncture gave but little fluid, two or three cubic centimetres at each puncture, sterile of micro-organisms. In this case unfortunately there was no post-mortem. In another case, which had lasted twenty-four days on admission, the puncture fluid revealed meningococci. In the fourth case, four months of age, admitted in the sixth week of the disease, the first puncture fluid was negative, the second revealed meningococci. In this case post-mortem examination confirmed the diagnosis. In the fifth case the puncture fluid revealed meningococci. In the sixth case, nine months of age, which sojourned in the hospital five months, a large number of punctures was made. The case was absolutely characteristic of the type described by Still, although no post-mortem was obtained. Hydrocephalus resulted and increased under observation. At one puncture no less than 250 c.c. of fluid were removed and yet the most patient search failed to reveal any micro-organisms. This being a chronic case, the cytology of the fluid was especially interesting. It resembled very closely what is seen in tuberculous meningitis. There was a mononuclear picture of leukocytes. I have explained this mononuclear picture elsewhere as being characteristic of so-called chronic cases of cerebrospinal meningitis.

In these cases, as in hydrocephalus, there is really a transudate rather than an exudate. The inflammation has run its course, but the hydrocephalus is the result of transudation of serum from the vessels rather than of exudation due to active inflammatory processes, and, according to Ribbert, a transudate would reveal a predominance of mononuclear lymphocytes.

In the second case, four months of age, there was a polynuclear picture, with sterile fluid. In the third case, four months of age, there was a marked polynuclear picture of the puncture fluid, and in this meningococci were found. In the fourth case, in which diagnosis was confirmed by post-mortem examination, there was a predominance of polynuclear elements in the puncture fluid, and in this case meningococci were found. In the fifth case, an infant nine months of age, the puncture fluid presented a polynuclear picture, and in this case also meningococci were found. It may be said, therefore, that the chronic cases yielded negative results so far as micro-organisms in the puncture fluid are concerned, and that the mononuclear picture resembled what is seen in tuberculous meningitis.

Post-mortem examinations were obtained in three of the six cases occurring in children below two years of age. In one, an infant six months of age, post-mortem examination showed that the superior surface of the brain was pale, that the convolutions were flattened, and that at the base there was a small amount of organizing, purulent exudate. The floor of the fourth ventricle was bulging and ready to burst. The foramen of Magendie was almost  $\frac{2}{3}$  cm. in diameter. The fluid aspirated from the ventricle showed meningococci. The



cord presented hemorrhages in the cervical, mid-dorsal, and lumbar regions.

The thymus was large, the lungs showed simple congestion, the heart muscle was pale, the spleen was moderately large, the Malpighian bodies quite large, and the liver was congested and somewhat fatty; the gall-bladder and duct were negative, the kidneys negative, the adrenals and pancreas negative; the stomach showed a few hemorrhagic areas in the fundus; the intestines showed follicular enteritis, swelling of the mucosa, vessels markedly injected, and the mesenteric nodes moderately enlarged.

In another case, an infant nine months of age, admitted on the seventeenth day of the disease, there was some purulent exudate over the vertex, but it was most marked at the base, completely surrounding the cord. There was considerable increase of the subarachnoid fluid, there was hydrocephalus, and marked dilatation of the ventricles.

In the third case, two years of age, admitted in the sixth week of the disease, post-mortem made at the end of the sixth week, examination of the brain revealed the dura adherent to the calvarium and the pia adherent to the dura mater over the motor areas on both sides. The brain was cedematous, with marked injection of the bloodvessels. There was an organized exudate of a yellowish-gray color on the surface of the brain. At the base, over the chiasm and anterior surface of the medulla and pons, and to a slight extent over the cerebellum anteriorly, there was a thick, grayish-yellow exudate. No tubercle. The ventricles were moderately dilated and contained some turbid fluid. The choroid plexus was congested, and a few petechiæ were scattered over the surface of the brain.

CASE I.—Male infant, aged four months; admitted May 31, 1904, in the twenty-fourth day of the disease.

*Family History.* Negative.

*Previous History.* Negative. Labor normal.

*Present History.* Child became ill twenty-four days before admission, with fever, crying out, painful rigidity of the neck, erythema over the general surface; eyes turned upward; no convulsions; occasional vomiting; fontanelles bulging; bowels and urination normal. There has been increasing loss of weight and slight cough. On admission, general condition fair, child well nourished. Head retracted to an extreme degree, no opisthotonos, feet drawn up on the abdomen, arms extended. Child cries when disturbed, otherwise quiet. Seems to notice objects. Sutures of the head still open, anterior fontanelle open and bulging; pupils react to light, no strabismus, no facial paralysis, no paralysis of the extremities. There is a Babinski reaction on both sides, often automatic; knee-jerks increased, no clonus; there is *tâche cérébrale*;

distinct trismus of the lower jaw, preventing a view of the throat. Skin, heart, lungs, liver, and spleen negative; abdomen rigid, without any palpable abnormality. There is shallow breathing, irregular in rhythm; pulse is of fair quality, but irregular.

Under observation there was occasional vomiting, this increasing until the child vomited after every feeding, always of projectile character. The rigidity and retraction of the head did not diminish. The fundus of the eye, examined by Dr. Gruening, gave a negative result.

On June 4 child's condition became worse to a marked degree; the pulse became very weak and rapid; the respirations, though rapid, continued irregular. The child took no nourishment, became slightly cyanotic, and lay with upper extremities in a condition of overextension, the fists clenched in the tetany position.

Lumbar puncture was made in this case on three different occasions, the first two punctures being negative, the third yielding 5 c.c. of a turbid fluid showing a marked preponderance of polynuclear leukocytes and numerous extracellular and intracellular Gram-negative diplococci, both by culture and stain.

The temperature in this case was normal until six hours before the exitus, which took place June 4, five days after admission. At this time, just before death, the temperature rose to  $105\frac{1}{2}^{\circ}$ . The range of pulse was very irregular—from 100 to 180 per minute. The respirations were irregular, ranging from 30 to 50 per minute. The leukocytosis in this case was 26,000 to the cubic millimetre. No post-mortem.

CASE II.—Male infant, aged four months; admitted to the service June 25, 1904, in the fifth week of the disease.

*Family History.* Negative.

*Previous History.* Negative, both as to infectious diseases and ear complications.

*Present History.* Infant became suddenly ill five weeks before admission, with fever, convulsions, and rigidity of the neck. Two weeks before admission the child went into a condition in which it lay quiet, with occasional contractions of the muscles of the arms and legs. At this time the mother noticed that the child no longer saw objects. Emaciation became marked, bowels constipated.

On admission, physical examination revealed an infant the general condition of which was poor. It lay very quiet, seldom cried. The head was retracted and there was some opisthotonos. The upper and lower extremities were adducted toward the trunk; the forearm, wrists, and fingers were flexed, the hands in the tetany driving position. The spastic condition of the lower extremities was so great that they could not be flexed beyond a slight angle, in which they were constantly held. There were periods of relaxation, however, in which the lower extremities could be flexed. The spastic condition of the upper extremities was very marked.

There were purposeless movements of the upper extremities, and a tendency to cross the legs. Reflexes at the knee were present, the great toe held in the Babinski position most of the time, but no true Babinski could be obtained; there was no clonus. The pupils reacted to light, of equal size; no strabismus. No facial paralysis. Anterior fontanelle prominent, posterior fontanelle closed; head not enlarged. No Macewen; ears and mastoid negative; marked signs of rachitis on the chest. Heart, lungs, liver, and spleen presented nothing of interest.

*June 26th.* Examination revealed an infant with body in a condition of spastic rigidity, with arching of the back, retraction of the head, with intervals in which the rigidity and opisthotonos are not so pronounced; fontanelles bulging; craniotables marked. A Babinski was obtained at this time; the hands still continued in the tetany position; arms rigid and extended; knees sometimes relaxed, at other times rigid. The occasional spasm which caused marked rigidity and arching backward of the head and body also affected the muscles of respiration, so that there was, when these spasms occurred, a crowing sound heard, formed in the larynx on inspiration. Trismus was present at times. A lumbar puncture was made on June 27, and 1.3 c.c. of a yellow, cloudy fluid obtained. The report on this fluid showed a cytological picture of a polynuclear type, but no meningococci. Spreads and culture negative.

The child died nine days after admission. During the whole stay in the hospital the temperature was normal with the exception of the second day, when it mounted to 101°. The pulse was very irregular, ranging from 104 to 150 during the stay in the hospital. The respirations ranged from 18 to 30.

CASE III.—Female infant, aged six months; admitted in the fourth week of the disease.

*Family History.* Negative. Mother has three other children.

*Previous History.* Negative, with the exception of a diarrhœa, at the age of two months, which lasted two weeks.

*Present History.* Infant has been sick four weeks. Illness began suddenly with fever and convulsions. Convulsions lasted two weeks and were repeated daily. Infant vomited once or twice. In the interval of the convulsions child lay perfectly quiet and did not cry. For the past two weeks there have been no convulsions. Mother thinks infant is blind and that the head is increasing in size. Slight cough for the last few days. Infant takes nourishment well. Bowels and urination normal. Child has lost in weight.

Physical examination shows condition good, well nourished; infant restless, head and extremities in constant motion. Skin presents nothing peculiar; small glands are felt in the neck and groin, none elsewhere. There is rigidity of the neck; no Kernig, no Babinski; knee-jerk present; no clonus; strabismus, pupils react to light, are equal, moderately dilated; no facial paralysis; tâche

cérébrale; tongue slightly coated. Heart, liver, and spleen normal. Abdominal wall rigid; abdominal contents present nothing peculiar. Child vomits its nourishment. Respiration irregular; at times child does not appear to breathe. Fontanelles bulging, head retracted. Child continued in this condition without very much change until just before death, which occurred quite suddenly.

While in the hospital on the first day the temperature reached  $101^{\circ}$ , on the second day  $102\frac{4}{5}^{\circ}$ , and on the third day of the sojourn in the hospital it dropped to normal and remained there until the exitus. The pulse was quite irregular, ranging from 100 to 130, respirations from 30 to 34.

Both eyes, examined by Dr. Gruening, showed optic atrophy.

Culture of the cerebrospinal fluid during life gave a negative result, but that removed after death showed meningococci and a polynuclear leukocytic picture.

*Post-mortem.* Thymus enlarged; lungs somewhat congested; heart muscle pale, foramen ovale open; spleen moderately enlarged, Malpighian bodies enlarged; kidneys negative; adrenals and pancreas negative; stomach, a few hemorrhagic areas in the fundus; intestines showed follicular enteritis, mucosa congested, and nodes enlarged. Brain surface pale, convolutions flattened; ventricles distended with fluid at the base a small amount of purulent exudate; floor of the fourth ventricle ready to burst, foramen of Magendie 2.3 cm. Cord showed hemorrhages in the cervical and dorsal regions underneath the pia.

CASE IV.—Female infant, aged nine months; admitted May 12, 1904, in the seventeenth day of the disease.

*Family History.* Negative.

*Previous History.* Negative, with the exception that there was a discharge from the right ear two months ago which lasted four weeks.

*Present History.* Infant was taken suddenly ill seventeen days ago, with fever,  $104^{\circ}$  according to the statement of the physician in charge. There was no cough and no convulsions. Rigidity and retraction of the head present for the last fifteen days. There was occasional vomiting; intestinal movements normal at first, but lately have become green, containing mucus.

Physical examination shows well-nourished infant; head retracted; neck rigid; pupils contracted, react to light. No Kernig, no Babinski; knee-jerks markedly increased; no clonus. *Tâche cérébrale*; hyperæsthesia; no meningeal cry; no rash on extremities, body, or mucous membranes. Fontanelles depressed. Respirations very irregular. Lungs, heart, and liver normal; spleen palpable below the borders of the ribs; abdomen relaxed.

Child continued very much in the same condition during its stay in the hospital, with the exception that on May 23d physical examination revealed the head more and more retracted, so that it formed

almost a right angle with the spine. Respirations shallow and very irregular, fontanelle not bulging; there is slight convergent strabismus; no facial paralysis. Child cries out without any cause, takes its food very poorly. There is marked *tâche cérébrale*, increased knee-jerks; opisthotonos is marked, though there are periods of relaxation during which the opisthotonos disappears. The retraction of the head, however, remains constant.

Examination of the blood showed leukocytosis ranging from 15,000 to 30,000 to the cubic millimetre.

Lumbar puncture revealed cerebrospinal fluid decidedly cloudy, showing a preponderance of polynuclear leukocytes, Gram-negative staining diplococci intracellular and extracellular both by spread and culture.

The temperature during the stay in the hospital was normal with the exception of the seventh day, when it rose, without apparent cause, to 101°, then dropped to normal, finally falling to subnormal just before death. The pulse was quite irregular, ranging from 80 to 160 per minute. The respirations were 20 to 38 per minute.

The urine showed amorphous urates and a few leukocytes.

Post-mortem examination, made of the brain only, showed a purulent exudate over the vertex and a marked exudate at the base, completely surrounding the cord. The ventricles were dilated and contained an increased amount of fluid. Brain not opened.

CASE V.—Female infant, aged nine months; admitted March 29, 1904, in the tenth week of the disease.

*Family History.* Negative.

*Previous History.* Difficult and prolonged labor. Child was born perfectly normal.

*Present History.* Infant was taken suddenly ill ten weeks before admission, with fever, stupor, and retraction of the head. The child continued from this time on with occasional fever and in a stuporous condition. Three weeks before admission it developed general convulsions, these convulsions being frequently repeated. The head became a great deal larger, there was a slight cough, and marked emaciation.

On admission the general condition of the child was very poor, emaciated, head retracted to extreme degree, marked opisthotonos. Forearm flexed on the arm, hands held in the driving position; lower extremities extended and the feet in the equinovarus position. Eyes prominent, head considerably enlarged, marked prominence of forehead and occiput; anterior and posterior fontanelles open, with bulging of the anterior fontanelle; separation of the bones of the cranium at the sutures. Macewen percussion note obtained on both sides of the skull. Incisors of the lower jaw present; slight trismus of lower jaw. *Tâche cérébrale*. Examination of the fundus of the eye negative.

This child was punctured eight times, from 40 to 250 c.c. of fluid

being withdrawn at each puncture. The puncture fluid was carefully centrifuged and repeatedly examined, with a view to finding meningococci, but none were found, nor were tubercle bacilli found. Cultures were made, with negative results, as were also injections into animals.

This infant was in the hospital six months, during most of which time the temperature was normal. There were periods, however, of a week in which the child ran a very irregular temperature, especially the first week of its sojourn in the hospital, when it ranged from subnormal to 104.6°. These temperatures were higher after lumbar punctures. After the second week the temperature remained normal.

The blood count, taken during the course of the disease, showed leukocytosis ranging, in the first week, from 9000 to 17,000, after which it remained low, not exceeding 10,000.

The pulse was very irregular, ranging from 100 to 160 per minute on different days. Respirations also were irregular both in rhythm and depth, ranging from 15 to 30 per minute.

Although the infant continued in the hospital for six months the head steadily enlarged in spite of the withdrawal of fluid. The emaciation came to a standstill at a certain point, and then the infant increased very slightly in weight, remaining thus until its withdrawal from the hospital.

Unfortunately there was no post-mortem, but the whole picture of the disease clinically was that of hydrocephalus following cerebrospinal meningitis, with extreme retraction of the head and opisthotonos which were constant, accompanied by tetany in the extremities and trismus of the jaw.

CASE VI.—Female child, aged two years; admitted April 25, 1904, in the fifth week of the disease.

*Family History.* Negative.

*Previous History.* Normal labor, breast-fed child. One year before admission had an abscess in the neck extending over three weeks; otherwise has been a bright, healthy child.

*Present History.* Five weeks before admission child was taken suddenly ill, with fever, general convulsions. Since the onset there have been, at times, remissions of the fever, though it has continued more or less up to the present time. The child has gradually become stupid, though the father thinks it is not blind. It vomits occasionally, and for the past three days there have been constant movements of the upper and lower extremities. The child has emaciated markedly. Bowels and urination normal. The father has noticed that the child's head has perceptibly enlarged during the illness.

Physical examination of the child shows that it lies with the head retracted, eyes wide open, head turned to the left. The body is arched and the neck rigid. There are occasional purposeless movements of the forearm and arms and sometimes of the lower

extremities. At times there seem to be coarse tremors of the upper extremities. The child starts at the least sound. The respirations are irregular and shallow. At times the extremities are held in a spastic condition, the feet being in a condition of extension, the arms flexed at the elbow, the fingers and toes flexed. In other words, the hands are clenched and the lower extremities are in a spastic condition similar to that seen in tetany. The pupils are equal, though widely dilated, but react to light. There is slight nystagmus. At times the arching of the back relaxes, but as soon as the muscles of the back are irritated the arching becomes extreme. Macewen's sign is marked, especially on the right side. The eyes show no optic neuritis or change in the fundus. Lung, heart, and liver negative; spleen congested, palpable below the free border; abdomen rigid, scaphoid in shape. On account of the trismus of the lower jaw the mouth cannot be opened or the throat examined.

Lumbar puncture reveals fluid in which there is an abundance of polynuclear elements, to the extent of 73 per cent., and 27 per cent. mononuclear. There are extracellular and intracellular diplococci not staining with Gram.

The child died suddenly without any change in the symptoms four days after admission.

The blood count the day after admission showed a leukocytosis of 19,200 to the cubic millimetre.

The temperature was normal during the child's stay in the hospital, with the exception of one day, when it rose to  $101\frac{1}{2}^{\circ}$  without any apparent cause. The pulse ranged from 100 to 140, and the respirations from 26 to 48.

Post-mortem examination showed that the dura mater was adherent to the calvarium and the pia mater to the dura mater over the motor areas on both sides. The brain was markedly œdematous, with pronounced injection of the vessels. There was a moderate amount of organized exudate of a yellowish-gray color on the surface of the brain. There was an increase of the subarachnoid fluid at the base of the brain; over the chiasm, anterior surface of the medulla, pons, and, to a slighter extent, over the cerebellum anteriorly, there was a thick, grayish-yellow exudate. The ventricles were moderately dilated, containing a turbid fluid. The choroid plexus was injected and there were a few petechiæ scattered over the surface of the brain.

Meningococci were found in the exudate at the base of the brain.

The above six cases are a series occurring in children two years of age and below, corresponding quite closely to what has been described recently by Still. All the clinical features of these cases were similar, and all presented the marked head retraction described by Gee, Barlow, Lees, and Still as characteristic of these cases. They all occurred in the course of an *epidemic of cerebrospinal meningitis* of a very extensive nature, prevalent among both children and adults,

and were admitted, with twenty-four other cases of cerebrospinal meningitis, to my hospital service. These cases were admitted at more or less advanced periods of their affection, as may be seen by reference to the histories, and none of them recovered. One case was discharged with increasing symptoms of hydrocephalus, as may be seen from the notes. It was, however, in a very poor physical condition at the time of its discharge.

The leukocyte count, as may be seen, was not very high in any case, and the lumbar punctures were unsuccessful in those cases in which the canal of Magendie was proved post-mortem to have been either narrowed or completely obliterated.

The question has arisen as to the exact causes of the peculiar features of these cases—that is, first, the retraction of the head, and, second, the hydrocephalus. Carr, in the *Medical and Chirurgical Transactions* of 1897, has attempted to explain the hydrocephalus as due, first, to obliteration of the foramen of Magendie, thus allowing an accumulation of fluid in the ventricles for which there is no escape; and second, to pressure of the exudate at the base, and in some cases thrombosis of the veins of Galen, resulting in a transudation or dropsy, so to speak, of the ventricles.

As to the retraction of the head, it has been explained by Still, and his predecessors as due to an irritation of the cervical nerves as they emerge from the intervertebral notches, thus causing a contraction of the smaller deep muscles of the neck.

Whatever the cause of the head retraction and the hydrocephalus in these cases, these two features are peculiar to them, and do not necessarily occur in forms of basic meningitis at a later period of life; nor does the fact that this form of meningitis is peculiar to infants necessarily exclude its occurrence at a later period.

I have been fortunate to observe a case of basic meningitis occurring in a boy five years of age, in which post-mortem examination revealed a typical meningitis of the Still type, due to streptococcus infection. In this case there was no retraction of the head; in fact, as will be seen from a study of the history of the case, the signs of meningitis were almost equivocal. Only slight rigidity of the neck, increasing stupidity, a Kernig sign, and the *tâche cérébrale* led to the suspicion that meningitis might be present. In other words, basic meningitis may occur at a later period in life without the characteristic symptoms seen in infants below two years of age.

**CASE.**—Basic meningitis due to streptococcus infection, occurring in a boy aged five years.

*Family History.* Negative.

*Previous History.* Normal birth; no traumatisms. Measles at age of one year; slight attack of pneumonia at two years of age. When four years old (one year before admission) he fell; was not unconscious, but was confined to bed for three weeks with high



fever, loss of appetite; vomited once, immediately after the fall; no other symptoms. Boy recovered completely.

*Present History.* The boy came under observation September 2, 1904. At that time he complained of headache and had a slight cough.

Examination revealed that the boy had febrile movement from  $103^{\circ}$  to  $105\frac{1}{2}^{\circ}$ ; pulse from 120 to 128; respirations 20 to 24. Examination of the lung gave equivocal signs. There was slight dulness over the right lung and diminished breathing behind.

Fever continued in the remittent curve from  $101^{\circ}$  to  $104\frac{1}{2}^{\circ}$ , and reaching  $105\frac{1}{2}^{\circ}$ . Respirations 20 to 24. Leukocyte count of 8000. Aside from headache there were no signs of meningitis before admission.

On admission of the boy to the hospital physical examination showed that he was slightly stupid, complained of sore throat, which was negative on inspection; temperature had the same curve, as noted above. There was dulness of the right lower lobe, behind and in the axilla; slightly diminished breathing. Heart was negative.

So slight were the signs of meningitis that the boy was rather suspected to have had typhoid, but the Widal test was made with negative results. The leukocyte count, however, mounted to 25,400. On the fourteenth day of the disease the boy became semi-stupid, developing rigidity of the neck and a Kernig sign. Lumbar puncture was made and a turbid fluid obtained, showing a preponderance of polynuclear leukocytes; abundant streptococci, both on spread and culture. The boy became more stupid, developed strabismus of the left eye, and there was considerable hyperæsthesia and irritability. Examination of the fundus showed optic neuritis of the left eye. Strabismus was supplemented with flatness of one side of the face. Patient developed conjunctivitis; the pupils were uneven and did not react to light. The lung developed a few subcrepitant rales over the upper part of the right lung in front and behind, with small areas of dulness. Spleen not palpable. Heart and liver negative. There was a leukocyte count before death of 18,000 to the cubic millimetre. The temperature of this case during the stay in the hospital was exceedingly irregular. It was of the remittent type, at times reaching  $104\frac{4}{5}^{\circ}$  and falling as low as  $99^{\circ}$ . On some days the temperature did not fall to normal; on other days it fell to normal, but immediately rose again to the figures mentioned. The pulse was extremely irregular, varying from 96 to 140 at various stages of the disease. The respirations were 24 to 32.

Post-mortem revealed a pure type of basic meningitis, the exudate at the base extending as far forward as the tips of the temporo-sphenoidal lobes. There was absolutely no exudate on the superior and lateral surfaces of the brain, although there was marked congestion of these areas. The purulent exudate did not extend down into the spinal cord. The ventricles were dilated and contained

a turbid fluid. Lungs showed hemorrhagic areas of bronchopneumonia scattered through both lungs.

Here was a case, it will be seen, of classical basic meningitis due to streptococcus infection, possibly from the lungs. A careful examination of the ears post-mortem throughout the bony construction showed absolutely nothing abnormal, nor could the avenue of infection be traced in this case. During life the symptoms of meningitis in this case were so non-characteristic as to lead two physicians whose powers of observation are undoubted to think of typhoid fever, or of some obscure disease other than meningitis. It was only in the later stages of the meningitis, when the stupor became evident and the rigidity of the neck marked, accompanied by Kernig's symptom, *tâche cérébrale*, and paresis of the facial nerves and ocular muscles, that meningitis was thought of. Lumbar puncture confirmed the suspicion. At no time in the course of the disease was there retraction of the head.

There are thus, according to the author's interpretation, two forms of basic meningitis. The first, which is primary, corresponds to the type described by Still, in which there is a primary inflammation of the meninges, as described in his paper, caused by the diplococcus intracellularis of Weichselbaum; and the second, occurring in older children, in which the symptoms in no way resemble those of the cases described by Still and the set described in this paper.

The cases occurring in older children may be complicated with pneumonia, as in the case last quoted, or may be secondary to a pneumonia. The characteristic symptomatology is evidently lacking, but there may occur certain symptoms which will point to a basic involvement, as in our case, such as facial paresis and paralysis of the muscles of the eye.

It is interesting, however, to note that cases of basic meningitis of the type described by Gee, Barlow, Lees, and Still may occur in epidemics of cerebrospinal meningitis, and be due to the same essential cause as the disease which occurs in older children. In fact, it seems that in the majority of cases of children attacked by cerebrospinal meningitis below two years of age the symptomatology is so closely allied—in reality identical—with that described by Gee, Barlow, and Still that the conclusion is inevitable that cerebrospinal meningitis, both epidemic and sporadic, in young children takes the form described by these authors in a certain set of cases.

NOTE.—The bacteriological and pathological data of this paper emanate from the pathological laboratory of the Mount Sinai Hospital, New York.

## USES OF THE ROENTGEN RAYS IN THE STUDIES OF NORMAL AND PATHOLOGICAL ANATOMY OF THE INTERNAL STRUCTURES OF THE FACE.

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THE closer the surgical anatomy of the face is studied by either the old stereotyped methods or the modern plan of sectionizing the parts in various directions, the more considerably it will be found to vary. The internal anatomy is not alike in two individuals; further than that, the two sides of the same individual are not alike. This condition often makes a true diagnosis and proper treatment most difficult. By the use of the Roentgen rays, by either the ordinary or the stereoscopical radiograms, much can be learned, both as to normal and pathological conditions.

The following illustrations will demonstrate the usefulness of radiograms:

Fig. 1 is made from one-half of a stereoscopical radiogram showing the general outline of the bone of two halves of the same cleaned dried mandible. Variations in the density of the cancellated tissue situated between the cortical portions of the bone are seen; also in the position and shape of the roots of the teeth with their nerve canals. The inferior dental canal can be plainly seen extending from the inferior dental foramen nearly to the apex of the canine tooth. In the upper picture an impacted lower third molar is visible, showing a pathological condition of the roots and those of the adjoining second molar; the roots of the impacted tooth pass backward just above the inferior dental canal, while in the lower picture the roots pass downward to the inner side of the canal. When the roots are in these positions they are liable to cause such pathological conditions as are exhibited in exostosis, both of roots and contiguous bone, and are also sources of other disturbances, such as neuralgia.

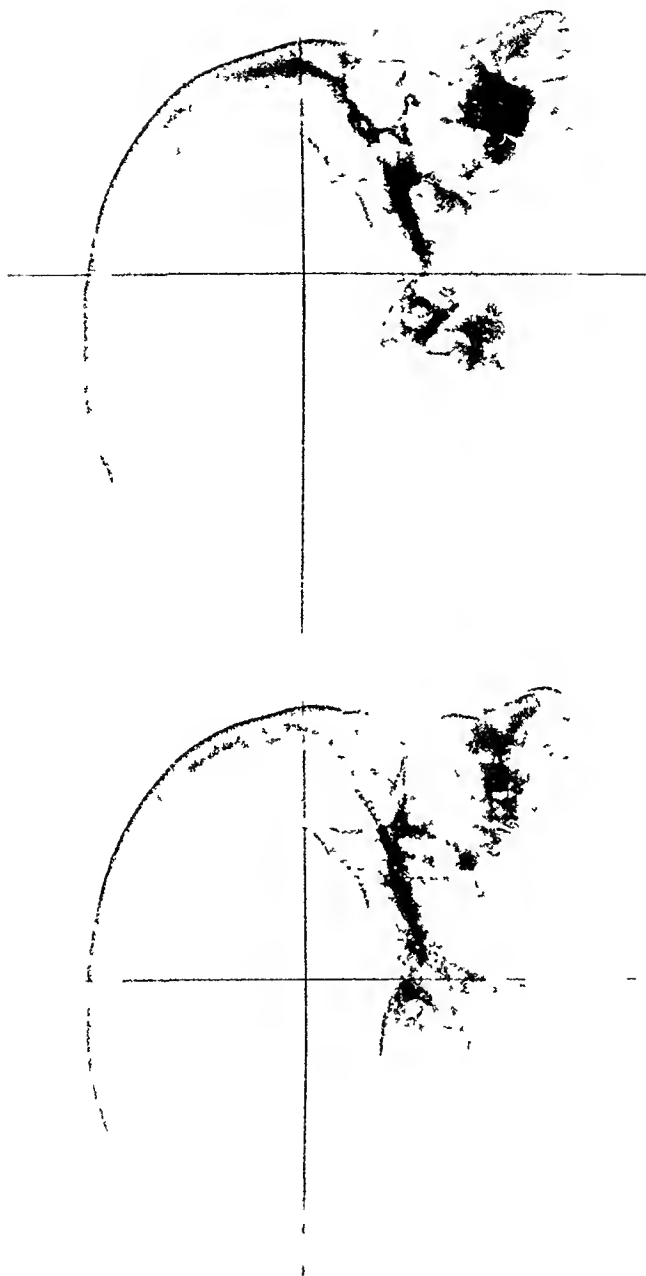
When the above picture is shown with its stereoscopical mate at normal size by reflecting stereoscope, the anatomical structure, with their positions, can be better studied.

During a visit to Dublin in the summer of 1903 the writer had the pleasure of seeing some stereoscopical radiograms made by Dr. William S. Haughton, to whose kindness he is indebted for the four illustrations which follow.

Fig. 2 is a stereoscopical radiogram of a cleaned or dried skull. The skull stands out in bold relief, the teeth and their pulp cavities and their relative positions as they are held in the alveolar process being clearly indicated. The upper third molars are impacted and rest on a line with the roof of the mouth near their place of develop-



FIG 2.



Stereoscopic radiogram.

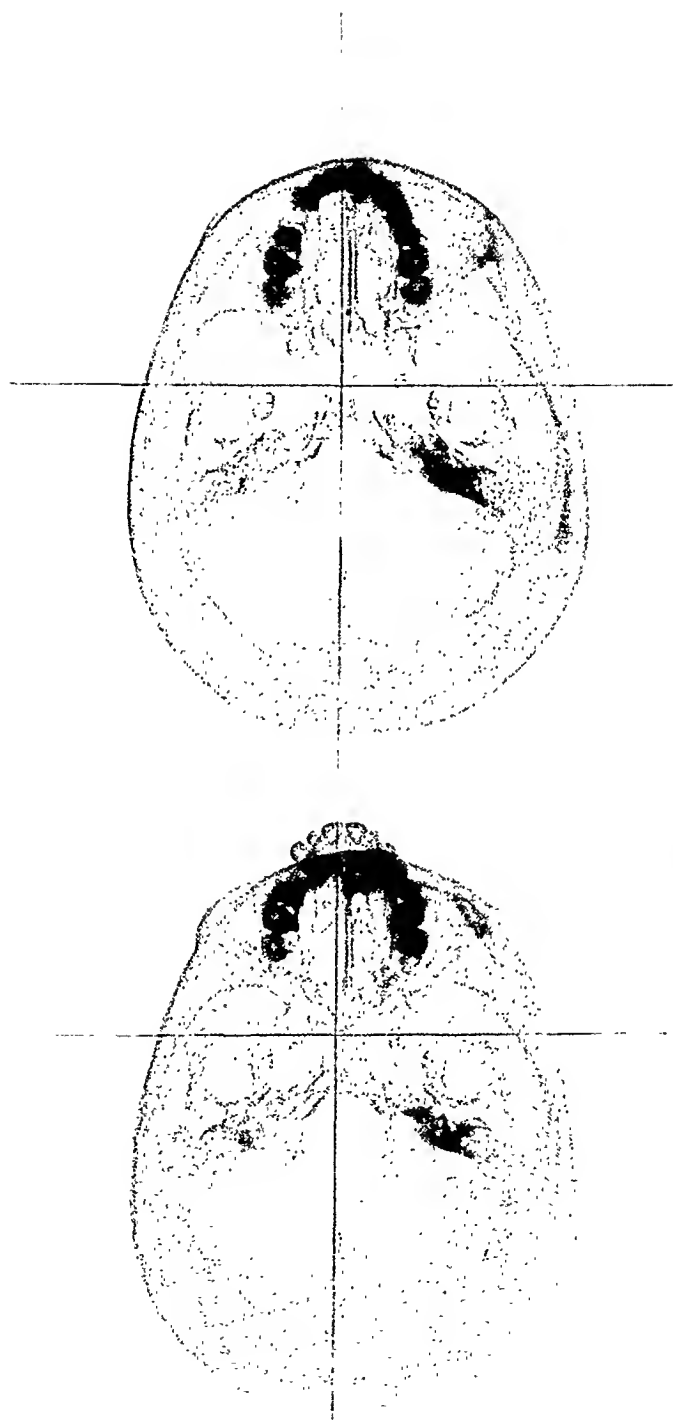
(To be examined with an ordinary prism stereoscope.)

FIG 3



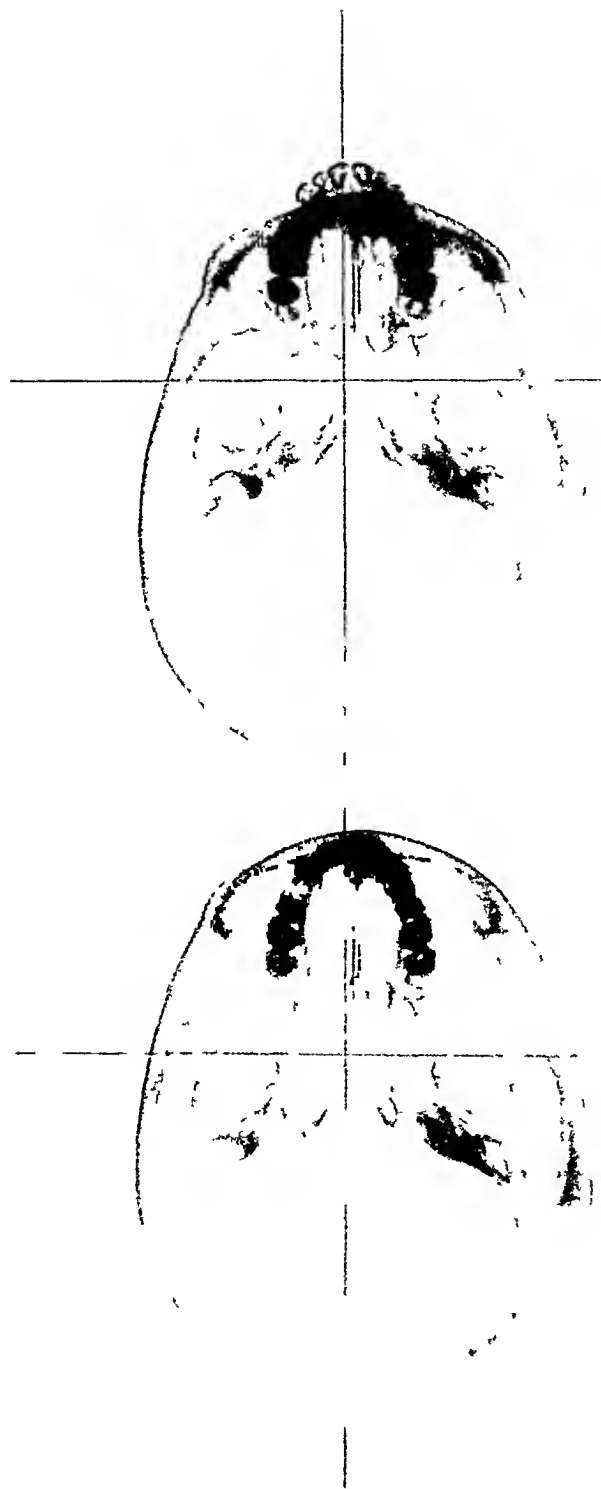
Stereoscopic radiogram, showing internal structures of skull.  
(To be examined with an ordinary prism stereoscope.)

FIG. 4.



Stereoscopic radiogram. Vertical view from base of skull.  
(To be examined with an ordinary prism stereoscope.)

FIG. 6.



Stereoscopic radiogram Vertical view from vertex.  
(To be examined with an ordinary prism stereoscope.)





ment. There is also an impacted upper premolar resting above the second premolar. In an ordinary  $x$ -ray picture it would be impossible to localize the true position of these teeth or of any foreign body, such as a bullet, etc., but with a stereoscopic picture they could be located. The region of the maxillary sinus is beautifully shown with a greater portion of the wall of the sinus. The floor of the boundaries of the orbit, its external wall, and the frontal sinuses, can be seen. Commencing with the right external angular process, the boundaries of the temporal fossa are all very well marked.

FIG. 1.



One-half of stereoscopic radiogram.

Fig. 3 is from the same stereoscopic radiogram as Fig. 2, the only difference being that the two halves of the stereogram have been changed in position. In Fig. 2 one is looking at the skull with the crossed wires in front of it, while in Fig. 3 the wires are beyond it. The latter view allows of a better study of the internal portion of the skull. The boundaries of the fossæ of the brain-case are well shown, and the free edges of the lesser wing of the sphenoid bone and the petrous portion of the temporal bone are markedly brought out. In looking through the skull to the opposite side of the brain-case,

the sutures are seen; also the grooves for the meningeal arteries. Above the body of the sphenoid the sella turcica is seen, and the sphenoidal sinuses are also shown in the body of the bone with the posterior ethmoidal cell in front of them. Within the petrous portion of the temporal bone the internal auditory meatus shows plainly, and back of the petrous portion is the deep groove for the lateral sinus.

Fig. 4 is a stereoscopical radiogram also by Dr. Haughton. It is a vertical picture taken through the skull shown in Figs. 2 and 3.

FIG. 6.



Sagittal section of a frozen head, showing the relation of the tissue at the base of tongue.

It gives a view of the base of the skull, the teeth, and the roof of the mouth. The position of the impacted teeth is well defined. Along the centre of the roof of the mouth are two lines showing the two plates forming the vomer and the other portions of the septum of the nose. The septum is straight, with a slight spur on the left side. The turbinated bones are seen through the roof of the mouth. Looking through the bone at the base of the malar bone and through the

tissues surrounding the teeth, the maxillary sinuses can be well defined. In passing back of the facial bones the internal structure of the basilar process of the occipital bone, and the petrous portion of the temporal bone can be studied.

Fig. 5 is from the same radiogram as Fig. 4, with the position of the two halves of the stereoscopic pictures changed from left to

FIG. 7.



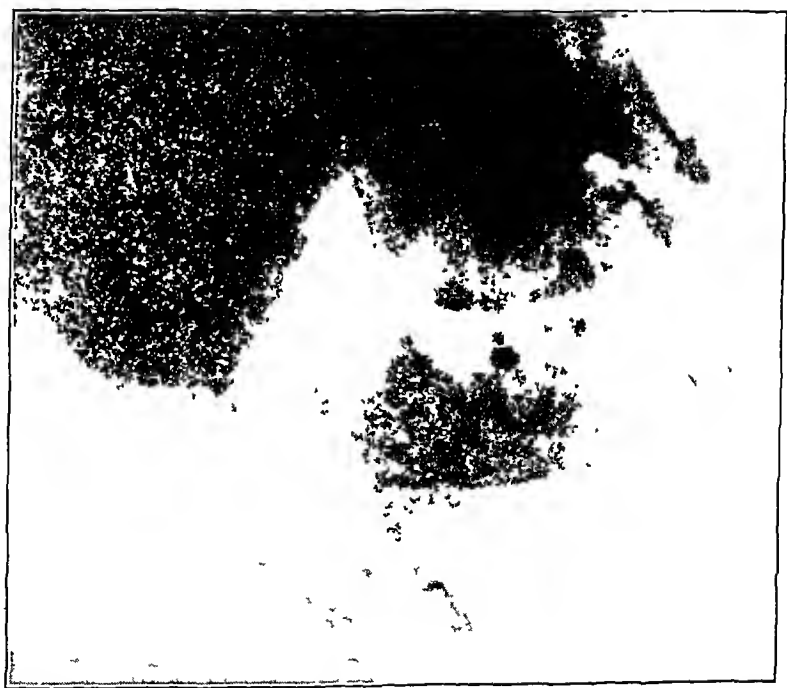
Radiogram, taken by Dr. Kassabian, of a living subject, showing the position of the eminentia articularis to the head of the condyle, when the mouth is wide open.

right and right to left. This gives a view of the skull from the top downward through the skull and out through the base, the exact opposite of that seen in Fig. 4. It shows the floor of the three fossae of the brain-case. The floor of the anterior fossa is somewhat indistinct, on account of its thinness, which allowed the  $x$ -ray to pass through it, but in so doing it reveals the ethmoid cells and the sphenoidal sinuses. Posterior to this position and extending out

laterally, the free margin of the lesser wings of the sphenoid are seen; also the middle fossa of the brain-case. The petrous portion of the temporal bone is well defined, with the various depressions along its ridge and two of its surfaces. Looking down into it the various cells and passageways are plainly visible. The mastoid cells are also shown.<sup>1</sup>

Much could be written about these four stereoscopic pictures, but enough has been given to indicate the many points of interest which can be studied without cutting the skull into sections. When penetrating rays of sufficient strength are used, similar features can be brought out in the living subject.

FIG 8.



Radiogram taken by Dr. Pfähler, showing an impacted lower third molar, with an inflammatory condition in the surrounding tissue.

**THE MOVEMENT OF THE MANDIBLE.** The general idea is that the mandible moves on a pivotal point within the glenoid cavity. From the study of the x-ray pictures of this bone taken from the living subject with the teeth in normal occlusion, with the mouth wide open, and in various positions between these points, it has been determined that the head of the condyle changes from one position to another. When the teeth are in occlusion, or nearly so, the con-

<sup>1</sup> The original four pictures as given to the writer by Dr. Haughton are little above the normal size, and when viewed in pairs by the use of a large reflecting stereoscope they show to a much better advantage than when reduced, to be used by the small prism stereoscope, as illustrated in this paper.

dyle rested in the anterior portion of the glenoid fossa, as seen in Fig. 8.

When the mouth was slightly opened the condyle seemed to be lowered a trifle and resting against the articular eminence. When the mouth was forced wide open the condyle was immediately under and resting against the eminentia articularis. In a few cases it was found slightly in advance of the eminence. In all cases examined, where the mouth was only slightly opened, the angle of the jaw moved slightly downward and backward.

FIG. 9.



Radiogram by Dr. Kassabian, showing necrotic condition of the ramus.

If the mechanism of the anatomy of the articulation of the lower jaw be carefully examined, it will be found that the internal, external, and stylomandibular ligaments act as suspensories to the jaw and have a tendency to fix its angle when it is carried slightly downward and backward, as when the mouth is partially opened. The muscular fibres of the internal pterygoid and the external portion of the masseter muscles have the same tendency. The condyloid process of the mandible acts as the fulcrum or pivotal point of the bone. The point, or fulcrum, mainly, through the action of the

external pterygoid, moves forward with its cushion, the interarticulating fibrocartilage. While the jaw is being carried forward the mouth can be opened slightly, still retaining the fulcrum, or pivotal point at the end of the condyle, but as the mouth is opened wider, the fulcrum is gradually changed from the condyle toward the more central portion of the ramus and then toward the gonion, the angle probably eventually becoming the fulcral point through the partial fixation of the ligaments and muscles before referred to. By the action of the external pterygoid muscle, the condyle is drawn for-

FIG. 10.



Radiogram.

ward, and the mouth is thrown wide open, with the condyle under or slightly in advance of the eminentia articularis, as shown in radiograms taken when the mouth is wide open. It is thus that the external pterygoid becomes an opener of the mouth. The reason for the change of fulcrum, or pivotal point, may be found in the condition which is obtained in the pharyngeal region. If in opening the mouth wide the head of the condyle acted within the glenoid fossa as the only pivotal point, the lower portion of the ramus with the body of the bone, the hyoid bone, the base of the tongue, and other associated tissues would be carried backward until the soft tissue

coming against the post-pharyngeal wall would interfere with the functions of that region. By the transfer of the point, this possibility is avoided.

Fig. 6 is made from a frozen section of a normal head, an examination of which shows the close relation of the posterior portion of the tongue and its associated tissues with the post-pharyngeal wall.

Fig. 7 was made from an  $x$ -ray taken while the mouth was wide open. It shows that the condyle has been carried well forward, with

FIG. 11.



True ankylosis of temporomandibular articulation.

its upper surface resting immediately under the eminentia articularis. This illustration shows other interesting points. The distal border of the ramus is anterior to the line of the vertebra, which is the normal position, even when the mouth is wide open. This point will be referred to again.

**PATHOLOGICAL CONDITIONS.** Fig. 8 is made from a patient of Dr. Dray, of Philadelphia, to whom the writer is indebted for this illustration. In the lower jaw the distal root of the second molar is covered by the crown of an impacted third molar. A cloudiness in this region indicates a condensation process, probably inflammatory,



which exists not only in the bone, but in the surrounding tissue. This is of vital surgical importance, as the patient was suffering from neuralgia at the time the picture was taken, and gave strong clinical evidence of the inflammatory condition in this region, which was caused by the *impacted lower third molar resting against the distal root of the second molar*. The absorption of the tissue of the root of the second proceeded until the pulp was exposed, thus causing the inflammatory condition noted. Upon the second molar being extracted, the inflammation and neuralgia subsided.

Fig. 9, taken June 25, 1904, shows a radiogram of the lower portion of the face. The ramus of the jaw was in a necrotic con-

FIG. 12.



The action of the superficial depressor muscles of the mandible in ankylosis.

dition. A steel probe could be passed into it at almost any portion. At the time the picture was taken, the probe was passed into the bone just below the coronoid process well through toward the temporomandibular articulation. The radiogram shows the probe in position, and also that the lower portion of the ramus was so decalcified that the x-ray passed through it (indicated by the light area). This picture was an important factor in making the true diagnosis of the condition.

Fig. 10 is another radiogram of the same patient taken on November 19, 1904. It shows that the light area of Fig. 9 has become more dense or regenerated, except a portion of the angle, which corre-

sponds to the clinical examination. The balance of the bone has become so dense that a sharp steel probe cannot be passed into it, as was done when the first picture was taken.

**TYPICAL SHAPE OF THE MANDIBLE AFTER A PERIOD OF ANKYLOSIS.** In 1898 the writer drew the attention of the profession to the fact that "the normal application of force to the developing bone results in the development of the form of the bone. The abnormal application of forces under the same circumstances results in the development of an abnormal form. Abnormal application of forces to bone in adult life will also change and modify its shape and character. The bones becoming changed, the whole body is modified according to the change in the tissue." The modification of bone by

FIG. 13.



Front view of a typical face of a person with an ankylosed jaw.

FIG. 14.



Profile view of a typical face of a person with an ankylosed jaw.

abnormal muscular action is well illustrated by the changes found in persons suffering from true or false ankylosis of the temporo-mandibular articulation.

In a paper written in 1898, Fig. 11 was used to illustrate the usual changes brought about in the lower jaw through the influence of ankylosis. In the same paper Fig. 12 was used to illustrate the action of the muscles drawing upon the bone in an endeavor to open the mouth. The person from whom Fig. 12 was made had been suffering from false ankylosis for about fifteen years.

Such changes in the form of the bone have been observed from time to time in various patients. Within the last few months a very interesting case has come under the writer's observation for consultation, which Figs. 13, 14, 15 and 16 well illustrate.

Fig. 13 gives a front view of the face, showing a heavy fold of tissue under the jaw, which would have been normal if the jaw were fully developed and in its normal place.

Fig. 14 is a profile, showing the recession of the mental process; also the "bagging" of the soft tissue, and below this are the mylohyoid muscles extending down to the hyoid bone, which has become displaced downward and backward.

Fig. 15 is another front view made when the patient was endeavoring to open the mouth. The lower lip and muscles are pulled down principally by the platysma myoides. The sternocleidomastoid muscles are well shown, also the sternohyoid.

FIG. 15.



Front view of a person with an ankylosed jaw when endeavoring to open the mouth

FIG. 16.



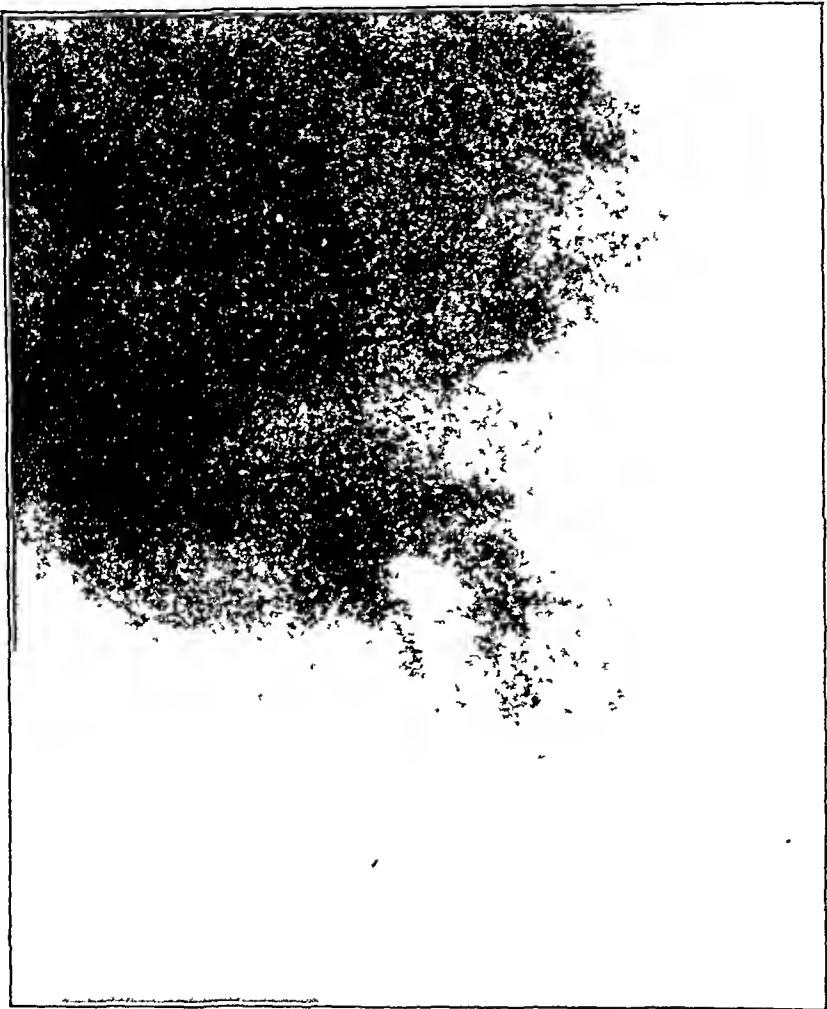
Profile view of a person with an ankylosed jaw endeavoring to open the mouth.

Fig. 16 is a side view, showing the side muscles in action. The platysma myoides and the omohyoid are well shown; a continuous line extends from the omohyoid to the jaw. This continuation in reality is the anterior belly of the digastric muscle. The action of these muscles can be studied from these last two pictures. Naturally, the anatomist and surgeon would be anxious to know something about the changes that have taken place in the internal anatomy through the muscular action. With this idea in view, two *x-ray* pictures were made, one from each side.

Fig. 17 is from a radiogram made from the right side, and shows that the mandible has changed completely, taking on the character of a typical ankylosed jaw (see Fig. 11), as was shown some eight

years ago, when the writer gave several illustrations demonstrating this point. This and other cases have confirmed the description and cause then given. The mental process is drawn back and the gonion downward. In this case the ramus is drawn back beyond a line parallel with the anterior portion of the vertebra. This may be partly due to the removal of the condyloid process in a surgical

FIG. 17.



Radiogram of a living subject, showing the typical slope of an ankylosed jaw.

operation. Through the loss of this process and with the action of the external pterygoid muscle, there is a tendency for the lower jaw to be forced backward; should it go back, the hyoid bone, the tongue, and all the tissues associated with it, must move backward nearly to or against the post-pharyngeal wall. All that prevents this tendency is the resistance exerted by the internal pterygoid muscles and

the external portion of the masseter. When the condyles have been removed and the external pterygoids severed from their insertions, the internal pterygoids and parts of the masseter have a certain amount of power to draw the jaw forward; also to rock it from side to side.

There are many other points of great anatomical interest in this picture. For instance, the dark line above the teeth is the roof of the mouth taken edgewise, which makes it look dense. Above this dark line are the maxillary sinuses. The line over this is in part the floor of the orbits, still above which is the region of the ethmoid cells. The roof of the orbits is outlined, and above that again the frontal sinuses are clearly seen, showing a septum between them. It would not do to claim that there was no septum, from this picture alone, as it is possible that it is there, and being thin, the rays have passed through it. Until lately the writer was of the opinion that there was always a complete septum between two frontal sinuses, but he has now in his possession two specimens without complete septa. If this person were suffering from disturbances in the frontal region, a radiogram, similar to this, might demonstrate the trouble. If the lower portion of the sinus should be filled with pus, it would be indicated by a darker shade than the upper. To prove that this dark portion contained fluid, it would be necessary to take another radiogram with the head at a right angle to the first position. Gravitation of pus would then change the position of the dark line, thus demonstrating the fluid nature of the contents.

If a stereoscopical picture had been taken of this subject and each half had been as good as the one shown, they would have proved of more value.

Radiographical pictures of dried skulls when shown by the stereoscope are all that can be asked for. But the surgeon will not be satisfied until the radiographer produces as good pictures from the living subject as those from the dried skulls. Sectionizing and the stereoscopical pictures have proved that no two skulls are alike in regard to the roots of the teeth, their shape, or position. The pneumatic sinuses and cells also differ greatly, therefore, when trouble exists in these regions and the surgeon is about to operate, he is anxious to know the special anatomy of the part to be operated upon, as to make a correct diagnosis is impossible without these. In such times the value of the  $x$ -ray is inestimable if the radiogram can be so perfected as to show density, shape, size, etc., in all their relations in a living subject. The writer is of the opinion that this knowledge will be obtained through the use of the stereoscopical radiogram. Those who are investigating along this line of work have accomplished a great deal during the past eight years since the discovery of the penetrating powers of the  $x$ -ray, and it is improbable that they have reached the limit.

## THE DEVELOPMENT OF THE ACCESSORY SINUSES OF THE NOSE.<sup>1</sup>

BY LEWIS A. COFFIN, M.D.,

SURGEON TO THE MANHATTAN EYE, EAR, AND THROAT HOSPITAL, NEW YORK..

I SHALL present a series of pictures illustrating the stages of development of the various sinuses, but before so doing I wish briefly to refer to the literature on the subject, quoting only such parts as apply to the time of the appearance of the various sinuses.

### THE FRONTAL SINUS.

Quain says: "The frontal sinuses appear about the seventh year and continue to increase in size up to old age."

Lothrop: "At birth the frontal bone is in two portions; the sinus has not yet appeared; the frontal eminences are prominent. As the child grows, the sinuses develop slowly and the general shape of the head and frontal region changes; at puberty the sinuses are practically developed and the frontal area has assumed its adult form." From a study of 125 skulls (250 sinuses) he found a frontal sinus always present, being confined to the orbital portion of the bone in cases in which by others it is said to be absent, this cell opening into the nose in conformity with one of the three modes of communication between the frontal sinus and the nose. This condition he found in about 3 per cent. of his examinations, at least on one side. I have in my possession a skull in which there is no cavity either in the vertical or orbital portion of the bone.

Turner says: "The sinuses (frontal) are not present at birth. Some difference of opinion has been expressed with regard to their first appearance. This is probably due to the fact that some observers record the period at which the sinus begins to develop, while others note the age at which the sinus is first recognized as a distinct cavity in the vertical portion of the frontal bone. It is generally held that the frontal sinus commences to develop at the end of the first year or at the beginning of the second year of life. As it extends upward and outward, expanding the frontal tables in its growth, it reaches in the sixth or seventh year above the frontonasal suture, and can be recognized at that age as a distinct cavity above the root of the nose."

The above, he states, are the observations of Steiner. He quotes Symington as reporting two cases in which fairly well developed sinuses were found at the age of nine and thirteen years. Symington did not find a frontal sinus in the vertical portion of the bone in

<sup>1</sup> Read before the Tenth Annual Meeting of the American Association of Laryngology, Rhinology, and Otology, at Chicago, May 30, 31, and June 1, 1901.

children under six years. Turner failed to find evidence of the sinus above the frontonasal and maxillary sutures in two cases, aged six and seven years. He warns against making deductions from a few observations, as sinuses are occasionally absent in adult life.

St. Clair Thompson (Posey and Wright) says: "The frontal sinus is absent at birth and during infancy; it is seldom evident before the seventh or eighth year." Dr. Thompson refers evidently to a distinct cavity in the vertical portion of the bone.

Kölliker says: "The frontal sinuses do not develop until after birth, and not fully until puberty. They continue to grow for a long time after."

Mouret says: "An absorption of the frontal diploë is produced at the same time the mucosa of the ethmoid diverticulum prolongs itself into the cavity for the purpose of lining it, prolonging the nasal cavity beyond the ethmoid."

It will be seen by the quotations given that there is some difference of opinion. Turner, Mouret, and others hold that the frontal sinus results from the upward expansion of the ethmoid labyrinth, while Lothrop, who has done an immense amount of work on the anterior ethmoid cells and the frontal sinus, sees, as I understand him, in the frontal sinus an independent cavity, always present and always opening independently into the nose.

In 1872 Steiner, with a considerable original work as a basis, contributed a valuable article on the development and anatomy of the frontal sinus. On its development he sums up thus: "The development of the ethmoid labyrinth at the end of the first year and beginning of the second year into gradually increasing spaces in the diploë of the nasal portion of the frontal bone is simultaneous with the growth of the frontal bone downward, so that at the sixth or seventh year we can find a frontal sinus about the size of a pea between the two layers of the frontal bone, as a result of the combined growth and out of which the diploë of the frontal bone fades away to be replaced by the cavities from the ethmoid labyrinth."

Dr. Steiner speaks of this resorption of the frontal diploë as due to pressure, but does not say from what source the pressure comes, whether it be the force of expansion from the natural development of the ethmoid labyrinth or whether it be a pneumatic pressure.

Tillaux is quoted by Steiner as stating that the frontal sinus develops from the eleventh to the thirteenth year. This Steiner has shown to be wrong.

It has seemed to me in my work that I have noticed that where there is obstructed breathing, especially from adenoid growths, there is a poor development of all the pneumatic sinuses, and I have wondered if in this we could not find the cause of the extension of the ethmoidal cells into the diploë of the frontal bone. We may have no frontal sinus, or one frontal sinus in any case, and it may

be developed as the result of the extension of the infundibulum or any other of the anterior ethmoidal cells (Mouret).

The diploë of the frontal bone manifestly is possessed of no inherent principle which causes its resorption. Neither does the capacity to expand into it seem to belong to any particular ethmoidal cell. It seems rather an accident. May it not be the weight or contiguity of the bone covering the various ethmoidal cells that determines which one is to prolong itself into the frontal bone? That is, given a cell with an incomplete or weak bony covering of its mucous lining, will it not expand under pneumatic pressure and, impinging on the diploë of the frontal bone, cause resorption of the cancellous tissue and the consequent cavity?

This peculiar development and expansion does not manifest itself either until just at that age at which children begin blowing the nose, etc., thereby causing increase of the intranasal pressure. The infundibulum is, I believe, usually a blind duct, limited at its upper extremity by mucous membrane only; hence it more frequently than any other cell pushes its way into and forms the cavity of the frontal bone.

#### THE SPHENOIDAL SINUS

Quain says: "The spongy bone begins to ossify in the fifth month. At birth each consists of the small sagittal lamina resting against the presphenoidal, continuing posteriorly into the lateral projection which is hollowed in front for the sphenoidal sinus, the latter having been formed as the recess of the mucous membrane of the nose at the end of the third month. By the third year the bone has entirely surrounded the sinus, forming an osseous capsule with an anterior opening—the sphenoidal foramen."

Turner simply states that the sinuses are not present at birth.

Symington says: "They begin to be formed as the spongy tissue of the bone about the third year. In a child of six he found them quite well developed."

St. Clair Thompson (Posey and Wright), speaking of their development, states that they are not present at birth. Their appearance is given by different authors as at the third year (Steiner), the seventh (Laurent), and the twentieth (Tillaux).

Sieur et Jacob (p. 379) say: "There are many opinions by different writers."

#### THE ETHMOIDAL LABYRINTH.

Turner, in his work on the frontal sinuses and ethmoidal cells, does not mention the *development* of the latter.

What Lothrop says of the embryology of the ethmoid bone would suggest that the cells first appear and grow by the development of pockets or diverticula from the cartilaginous nasal wall during the early years of infancy.



Quain says that the ethmoidal cells appear in the sixth month as depressions of the mucous membrane, but bony walls are not developed until after birth.

Köl liker says that the ethmoid cells are already hollowed out in the foetus as early as the sixth month; at birth they are well marked.

#### MAXILLARY SINUS.

The maxillary sinus exists at birth, having at that time, according to Turner, the following measurements: "Vertical diameter, 3 mm.; transverse diameter, 7 mm. In infancy and early childhood this small sinus occupies a position relative to the orbit entirely different

FIG. 1.

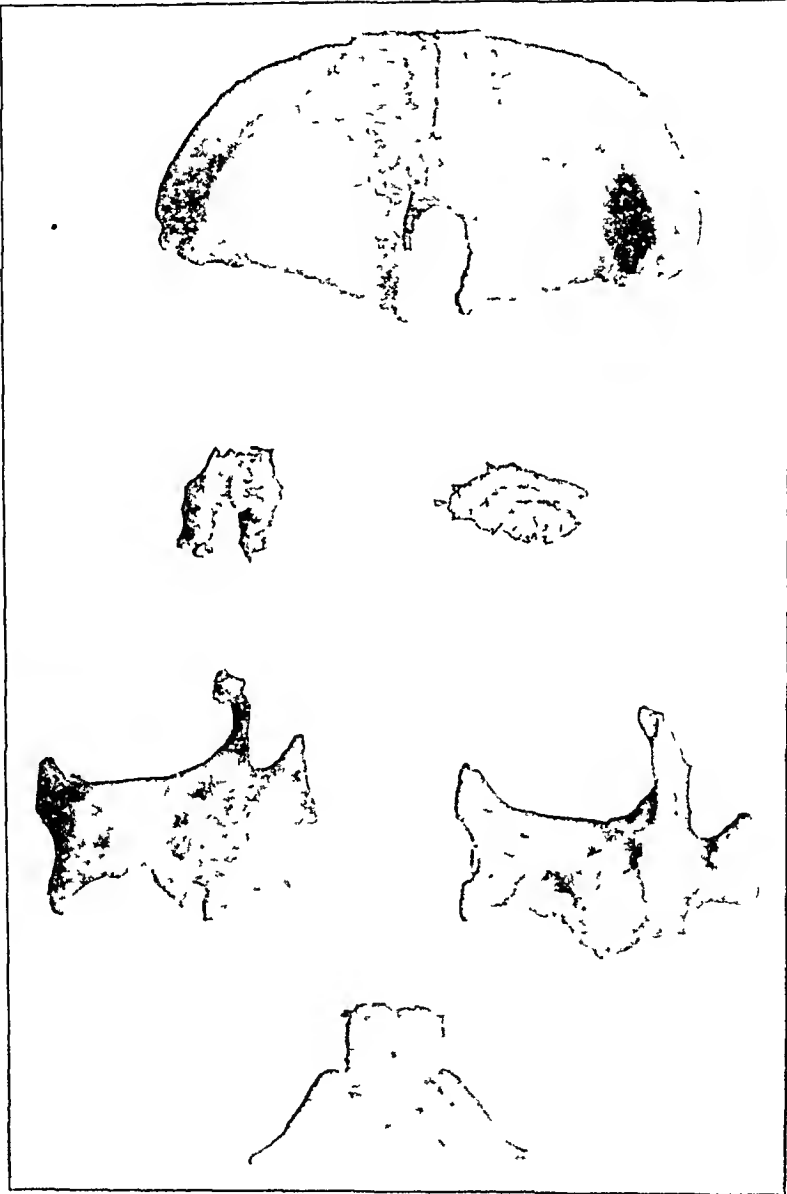


from that occupied when fully developed. At this period the body of the superior maxilla is made up almost entirely of the articular bones of the jaw, the sockets of the teeth being almost in contact with the orbital plate of the maxilla forming the floor of the orbital cavity. There is, therefore, at birth no maxillary sinus beneath the orbit."

Knowledge of this fact is of the utmost importance in diagnosing and treating infraorbital empyema in the infant.

The discrepancies of different writers and the expression by them of the uncertainty of the time of appearance of the various sinuses,

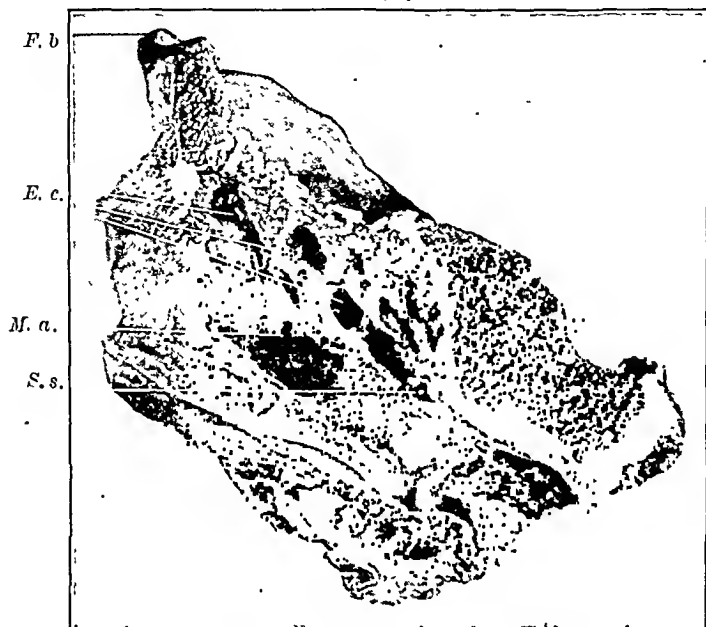
FIG. 2.



together with the confusing of the time of appearance of a sinus with the time of its full development, by students and workers in rhinology, I take it, is largely responsible for the fact that little attention has been paid to sinusitis in children.

For practical purposes from my own experience in the examination of from twelve to fifteen skulls of infants and stillborn, from the sixth month on, and from a review of the literature on the subject, the following deductions may be made:

FIG. 3.



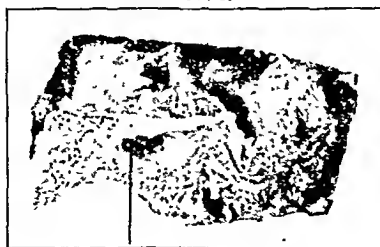
*F. b.*, frontal bone. *E. c.*, ethmoid cells. *M. a.*, maxillary antrum. *S. s.*, sphenoidal sinus.

1. But two of the accessory sinuses are present at birth—viz., the ethmoidal cells and the maxillary antrum.

2. The ethmoids and the antrum are constant sinuses.

3. The antrum does not in infancy occupy the same relative position in regard to the orbit as in later life, and cannot be reached or entered by the usual methods; neither can this be done nor

FIG. 4.



*S. s.*

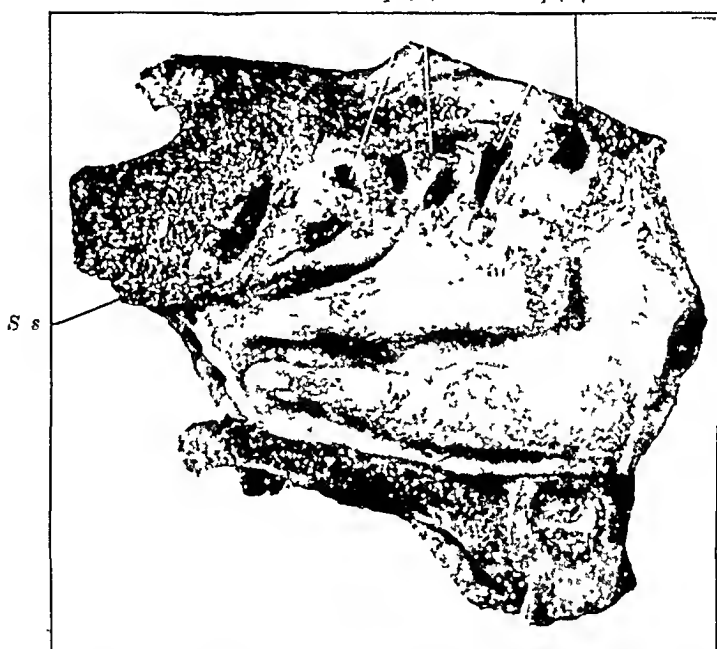
satisfactory drainage effected until after the descent of the second or permanent teeth without the destruction of a tooth socket. It makes impossible also the antral route to the ethmoid and sphenoidal sinus during this period of life.

4. The sphenoidal sinus makes its appearance shortly after birth, and may be found as a distinct cavity as early as the end of the first year. Practically, however, it may be considered as the most posterior of the posterior ethmoid cells.

5. The frontal sinus is not present at birth. It appears first in the orbital plate of the frontal bone between the end of the first and the beginning of the third year. Practically at this time it is the most anterior of the anterior ethmoidal cells. As I shall illustrate, it may be seen in the vertical portion as early as the end of the third year. This is early, however, and its appearance in the vertical portion should be put down from the third to the sixth or seventh year. I have opened and operated upon the frontal sinus

FIG 5

P e c      l e c



A e c, anterior ethmoidal cells. P e c, posterior ethmoidal cells

of a boy nine years of age which was considerably larger than the cavity of a large almond.

The accompanying figures illustrate the stage of development of the various sinuses at different ages from the six months' foetus to the adult.

Fig. 1 represents the sinus-containing bones of a seven months' foetus. At the top are the two lateral masses of the ethmoid. On the next line are shown the two superior maxillary bones, the one on the right showing the nasal aspect with the antrum just posterior to the nasal process on the inner side of the orbit. On the left the bone is so posed as to show the comparatively enormous size of the tooth sockets. Below is the sphenoid bone minus the greater wings.

Fig. 2 shows the sinus-containing bones of a seven months' child. At the top is the frontal bone with nasal bones in articulation. Below and to the left is the ethmoid bone. To its right is seen, wrong side up, the nasal aspect of the lateral mass of another child of the same age. On the third line are posed the two superior maxillary bones in the same position as in Fig. 1. At the bottom is the sphenoid bone.

FIG. 6.

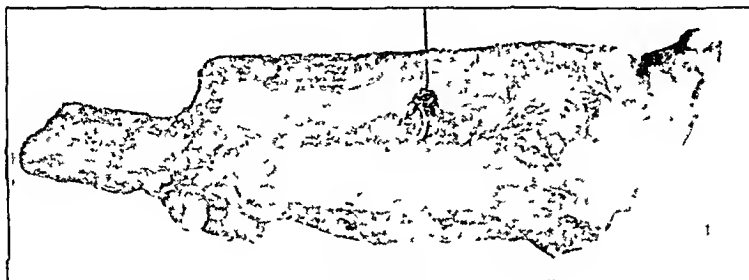
*F s**F. s.*, frontal sinus.

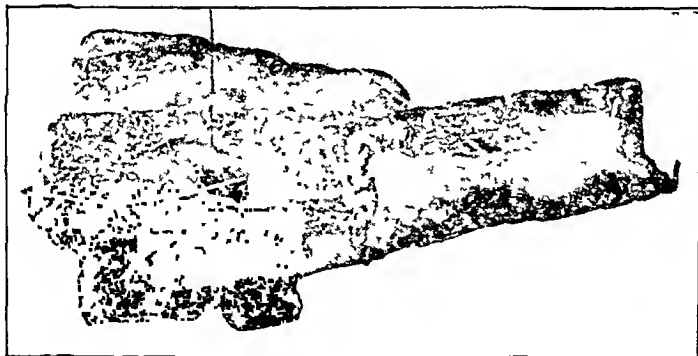
Fig. 3 shows the external wall of the right nasal fossa of a child one year old, the middle and superior turbinates having been removed.

Fig. 4 shows the section through the sphenoid bone, showing the sphenoidal sinus in a child one year of age.

Fig. 5 shows the external wall of the left nasal fossa of a child three years of age, the superior turbinated having been removed to show the size of the ethmoidal cells. In the back can be seen

*S. s.*

FIG 7



the sphenoidal sinus. The sinuses of this child seem to be well developed, and in passing I wish to call your attention to the unobstructed nasal pharynx.

Fig. 6 shows the horizontal section through the frontal bone of a child three years old, showing a cavity well within the cancellous tissue of the bone, above the frontonasal suture.<sup>1</sup>

<sup>1</sup> Since this paper was written Lothrop has reported having found a well-developed frontal sinus in the skull of a four-year-old child.

Fig. 7 shows the sphenoidal sinus in same specimen as Figs. 5 and 6.

Fig. 8 shows the external wall of the right nasal fossa of a child three years old, having middle and superior turbinateds removed.

FIG. 8.  
F. b.

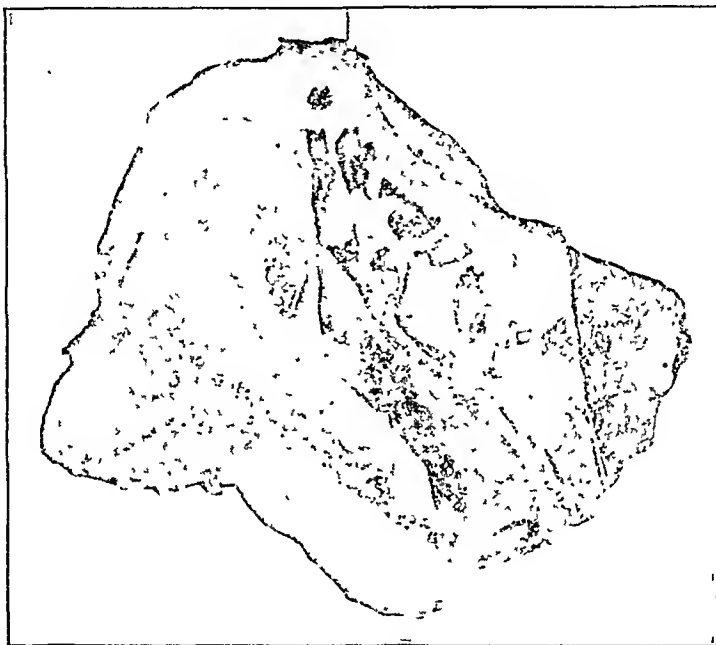
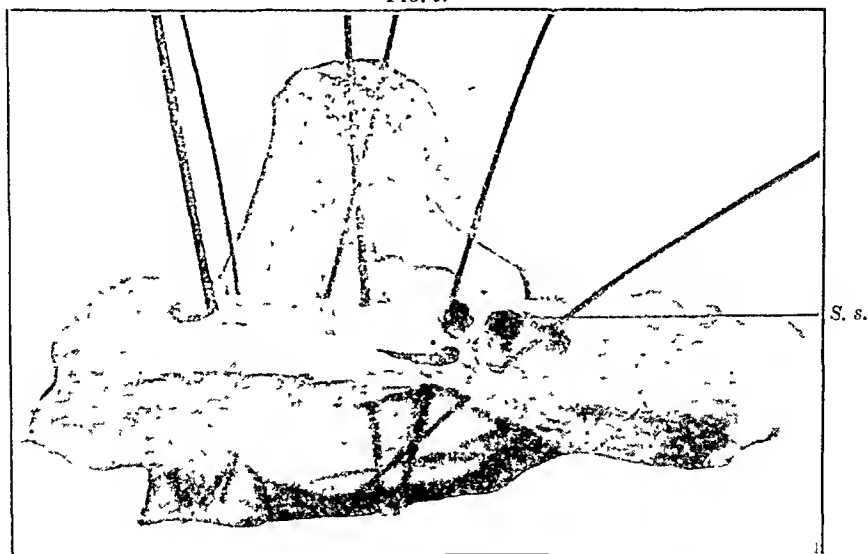


FIG. 9.



*M. t.*, middle turbinated bone. *S. s.*, sphenoidal sinus.

A bristle is seen passing from the infundibulum out through a cavity in the cancellous tissue of the frontal bone.

Fig. 9 shows the external wall of the right nasal fossa of a child

three years and eight months of age. Horizontal section has been made through the ethmoidal region so as to uncap these cells and

*F b* FIG. 10.



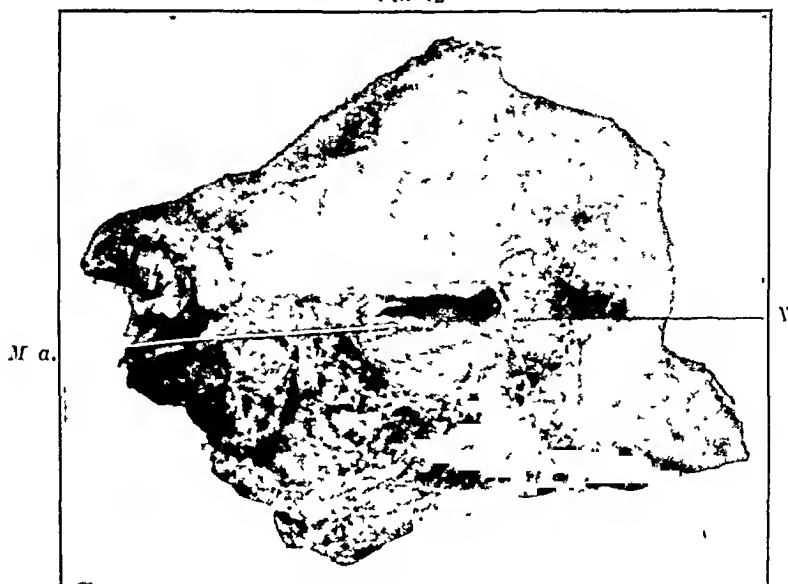
*F. b* , frontal bone    *A e c* , anteriorethmoidal cell, bony wall removed    *A* , adenoid growth

*A e c* FIG. 11 *A e c*



the sphenoidal sinus. The bone is tilted over so as to show the external wall of the nasal fossa and the ethmoidal cells and sphenoidal sinus.

FIG 12



*X*, top of tooth socket. *M. a.*, maxillary antrum

FIG. 13



*I. f.*, infraorbital foramen. *T*, top of tooth.

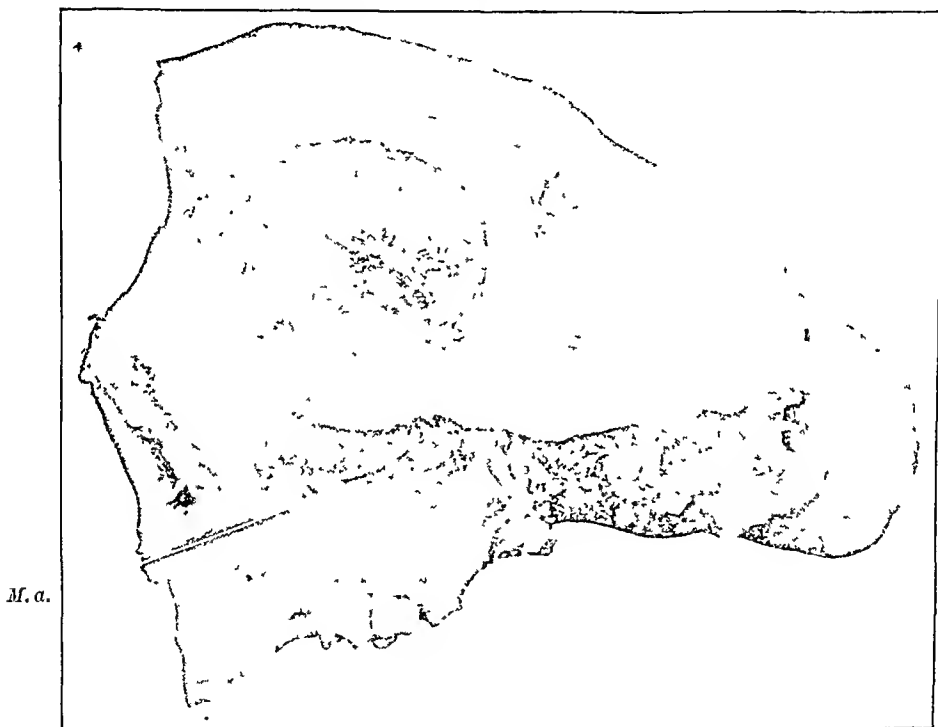
noidal sinus on the top. Bristles passing through the anterior ethmoidal cells are seen to emerge below the middle turbinated,



while those through the posterior cells and the sphenoidal sinus emerge above the middle turbinated. Cells are well developed. This child had a perfectly free nasopharynx.

Fig. 10 shows the right nasal fossa through the fenestrated nasal septum, anterior half of middle turbinated having been removed to expose the hiatus semilunaris. Through this gutter the anterior ethmoidal cell has been packed with red worsted. A coronal section has been made through the vertical portion of the frontal bone and the anterior flap turned out to show zone of compact bone through centre of cancellous tissue. This may illustrate the formation of the bony septa so frequently found in the frontal sinus.

FIG. 14.



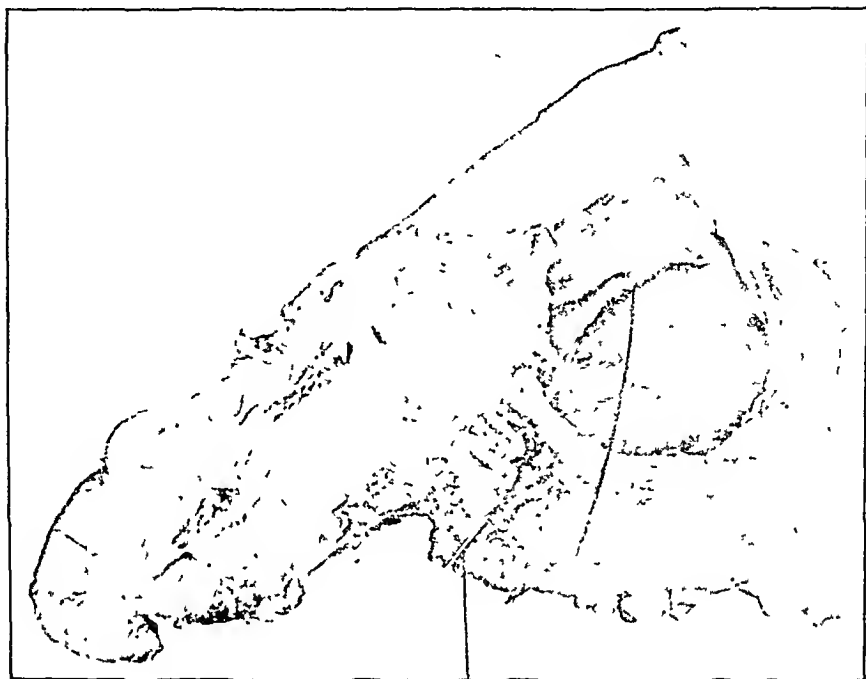
There is no frontal sinus in this case. The specimen is from a child seven years old, and the nasopharynx is to be seen much encroached upon by adenoid growths.

Fig. 11 shows horizontal section through the ethmoid region of the left side of the head and from the same child as Fig. 10. I wish especially to call your attention to the poor development of all the pneumatic cells in this specimen.

Fig. 12 shows the antrum in a child three years old opened through the external wall of the superior maxillary. The dark line drawn on the picture indicates the top of the tooth socket of the second or permanent tooth.

Fig. 13 shows the anterior surface of the superior maxillary bone from a child seven years of age. Second teeth have not come down

FIG. 15.



A.

A, adenoid mass.

FIG. 16.

X.

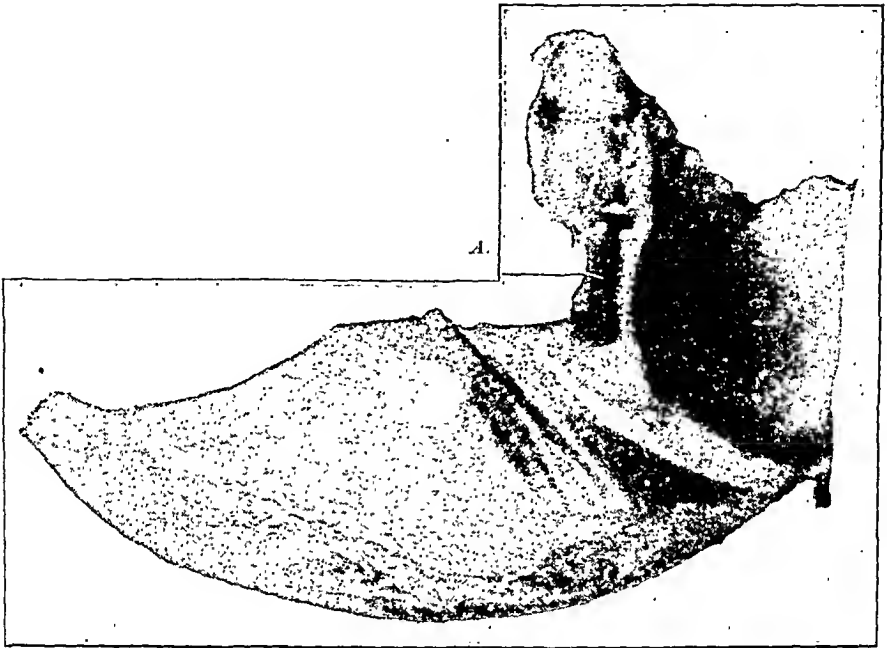


X, lining membrane of frontal sinus.

and the top of canine tooth can be seen in the notch immediately below the infraorbital foramen. This picture is shown to illustrate

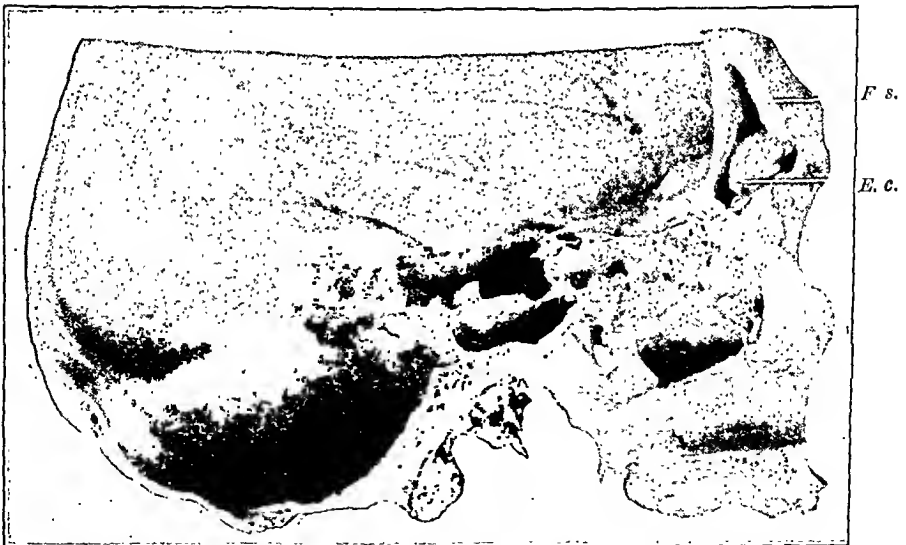
how small a space we have for operating on the antrum even in a child seven years of age.

FIG. 17.



A., depression between orbital plates.

FIG. 18.



F. s., frontal sinus. E. c., ethmoidal cell within frontal sinus.

Fig. 14 shows the external surface of the superior maxillary of a child nine years of age. The anterior wall of the antrum has been removed, leaving the mucous lining *in situ*. This illustrates how

much greater space is had for operating on the maxillary antrum after the descent of the second or permanent teeth.

Fig. 15 shows the external wall of the left nasal fossa through the fenestrated septum in a child nine years old, the middle turbinated and anterior half of the superior turbinated having been removed. The bristle seen passes through the infundibulum into the anterior ethmoidal cell. There is no frontal sinus. I wish to call attention to the enormous adenoid mass in the vault of the naso-pharynx. All the sinuses in this child were poorly developed.

Fig. 16 shows the external wall of the right nasal fossa of a child nine years old. The specimen has been so posed as to look distorted, but that is only for the purpose of showing the extent of the

FIG. 19.



*E. c.*, ethmoidal cell, filling frontal sinus.

frontal-sinus development. The lining membrane of the frontal sinus has been dissected away from the bone and may be seen in the upper left-hand corner of the figure.

Fig. 17 shows the frontal bone of an adult in which no frontal sinus could be found unless the depression seen between the two orbital plates of the frontal bone be so considered. It is very shallow and is merely the complement or the external wall of an anterior ethmoidal cell.

Fig. 18 is from a specimen kindly loaned me by Dr. H. M. Flower, of Toledo, Ohio. It shows an interesting condition in the frontal sinus. The frontal sinus is large and contains a very large ethmoidal cell. This figure illustrates how easily one might get into trouble even from an external operation for a frontal sinusitis. At the ordinary point of opening one would enter immediately this large

ethmoidal cell and might easily satisfy himself that he had cleaned out the entire frontal sinus without even having entered it.

Fig. 19 is from the other half of the same head as Fig. 18. In this picture an ethmoidal cell is seen to fill completely the frontal sinus of this side.

## A CASE OF PARINAUD'S CONJUNCTIVITIS.<sup>1</sup>

BY WILLIAM CAMPBELL POSEY, M.D.,

OF PHILADELPHIA.

ON October 20, 1898, I was consulted by Dr. X., a surgeon of volunteers, who had just returned from Porto Rico. While there, in charge of one of the hospitals, he had contracted an inflammation of his right eye, which he thought was of a gonorrhœal nature, as many cases of that disease were under his care when the eye became affected. When the eye was first inflamed, he said that the lids were swollen and were bathed in quite a copious mucopurulent secretion. The conjunctiva was also swollen and was studded with granules not unlike those of granular conjunctivitis. The inflammation of the eye, however, was not of the violent type which is usual in gonorrhœal ophthalmia, and did not interfere with his continuing his surgical duties. Washes of boric acid were employed, and the eye was cauterized upon several occasions with nitrate of silver. Notwithstanding this treatment, the inflammation of the eye persisted; the fellow-eye, however, remained unaffected. About three weeks after the appearance of the ocular inflammation a swelling was noticed in one of the small preauricular glands, and shortly after this the parotid gland itself of the same side was found to be affected. Signs of suppuration developing in the gland, an incision was made into it, and exit given to a small quantity of pus. Shortly after this, as the ocular inflammation persisted and his general condition was below par, he was sent home for further treatment.

When first seen by me, six weeks after the first appearance of the ocular symptoms, it was noted that both the upper and the lower lid of the right eye were much swollen, and that their edges were moistened by a slight mucopurulent discharge. Upon eversion of the lids the swelling was found to be occasioned by a marked thickening of the conjunctiva, especially in the folds occupying the fornix of both lids. From these folds were hanging a number of granulations which were much enlarged and were distinctly pedunculated, being at least an eighth of an inch long; between these were smaller granulations, which presented somewhat of a

<sup>1</sup> Read before the Ophthalmological Section of the College of Physicians of Philadelphia, October 15, 1904.

gelatinous appearance. The bulbar conjunctiva was injected and thickened, especially in the region of the caruncle. The cornea was unaffected. A bacteriological study of the conjunctival secretion, which was made by Dr. S. S. Kneass, was negative. The parotid gland was swollen and tense, and the submaxillary and retromaxillary and some of the cervical glands were also enlarged. The patient was admitted to the Presbyterian Hospital, by Dr. Henry R. Wharton, for the purpose of incising the parotid, which was swollen and showed signs of suppuration. This operation was accordingly performed under ether, when it was discovered that the gland had degenerated, though but a small amount of pus was evacuated. Ice compresses were prescribed for the eye, the conjunctival cul-de-sacs were flushed frequently with boric acid solution, and silver nitrate was applied daily. Under this plan of treatment the ocular condition slowly improved and the swelling of the conjunctiva subsided, though the granulations with their long pedicles still persisted. The patient's general condition was, however, poor, his temperature being decidedly elevated, and his condition one of exaggerated depression. Upon this account Drs. Musser and Sailer were placed in charge of the case, and so continued until convalescence was complete, which did not happen until the expiration of three months. A further report of the general medical aspect of the case is unnecessary here, further than to say that it was positively determined by both of these clinicians that Dr. X. was the subject of Malta fever. Their report of the case may be found in the *Philadelphia Medical Journal* for December 31, 1898, and July 8, 1899. It will not be necessary to say more of the ocular condition than that the subsidence of the inflammation and the total disappearance of the granulations were gradually attained after a period of six to eight weeks of active treatment. No scars were left in the conjunctiva, and the eye made a perfect recovery.

There can be no question, I think, but that the case which has just been reported is an instance of that rare variety of conjunctival disease known as Parinaud's or infective conjunctivitis. The first description of this form of disease was given by this distinguished French ophthalmologist in 1889, before the Ophthalmological Society of Paris. Since then a few other communications have been made upon the subject, although now, fifteen years after the description of the disease, the literature contains but twenty-three cases. Although a very comprehensive paper upon this subject by Chaillous, in the *Annales D'Oculistique*, of January of this year, and its able review and translation by Mr. Elmore Brewerton in the *Ophthalmic Review* of last May, and a very recent article by Verhoeff and Derby,<sup>1</sup> render any attempt of mine at

<sup>1</sup> Archives of Ophthalmology, July, 1904.

a detailed study of this form of conjunctivitis and its literature unnecessary, it may not be amiss, in view of the fact that the disease is almost entirely unknown in this country, and as the cases reported before the section to-night are, as far as I know, the first which have been seen in this city, to mention a few of its chief characteristics.

The first symptoms are those of a mild case of granular or purulent conjunctivitis. The secretion is not very abundant, the lids are swollen, the conjunctiva thickened, and granulations appear, which are at first small and semitransparent, then become yellowish and later red and opaque. In most cases some of the granulations assume a polypoid character, and may attain one-quarter of an inch or more in length. These granulations, hanging chiefly from the fornix, present a most striking appearance, and form one of the characteristic features of the disease. If the granulations be separated with a probe small erosions will be found lying between them, as well as minute yellow granules, which resemble those seen in tuberculosis of the conjunctiva. The bulbar conjunctiva is injected and often œdematous. The cornea is unaffected and the disease is almost always confined to one eye. Shortly after the ocular symptoms manifest themselves, although in a few cases preceding them the preauricular and parotid glands and at times the submaxillary and retromaxillary glands of the same side as the affected eye become swollen and indurated, and not rarely break down and suppurate. The general system always shows signs of depression, and there is some fever throughout the course of the affection; its onset may be inaugurated by a distinct chill. The disease is essentially chronic, both ocular and granular symptoms persisting and resisting treatment for weeks and months, though if left to itself it will undergo spontaneous cure without leaving scars in the conjunctiva. But little pain is experienced, either from the swollen lids or the enlarged glands. The disease is non-contagious.

The symptoms of the disease are so striking that it cannot readily be confused with any other form of conjunctivitis, except perhaps tuberculous conjunctivitis. It simulates this latter disease very closely, and though the simultaneous involvement of the glandular system, and the peculiar pedunculated character of the granulations in some cases, and the rather characteristic erosions which occur between the granulations, will usually enable the diagnosis to be made from tuberculous conjunctivitis without any great difficulty, yet in other cases the result of histological examinations and of experimental inoculations will have to be obtained to make the differentiation absolute. Though bearing a certain resemblance to trachoma, it can easily be differentiated from that form of conjunctivitis by the more diffuse character of the infiltration, the length of the granules, the non-affection of the cornea, and the involvement of the glandular system.

Although the small number of cases which have been thus far recorded renders any conclusions regarding the nature of this peculiar form of conjunctivitis of no great value, it is of interest to note that from the analysis of the twenty-three hitherto reported cases, Verhoeff and Derby found that the disease has thus far been observed only in the temperate zone and in climates not differing to any marked extent; that autumn seems to present the most favorable conditions for its development; that the sexes are affected equally often; that the age limits range from two to fifty-nine years; that the right eye was affected twice as often as the left.

The origin of the affection is still unknown. Parinaud thought that it originated from decayed animal matter and termed it "infective conjunctivitis," but as this observation was based solely upon the coincidence of the disease originating in some of the cases observed by him in subjects who were more or less exposed to infection of such a source, and though a possibility of infection under similar conditions has been reported by others, yet the bacteriological proof of this, though carefully and repeatedly searched for, has not been found. Gifford, who has reported five cases of the affection and has recently written me that he has seen four or five additional, does not believe that Parinaud's grounds for his belief are sufficient; and Chaillous, while he admits the probability of the infective nature of the process, suggests that the variations which are observed in the localization of the affection, in the vegetations and erosions, and in the reactions of the lymphatic system, indicate the action of varied infective agencies. Verhoeff and Derby, who have made a most careful bacteriological and histological examination of their case, and who have studied the literature of the affection with particular care to the elucidation of this point, conclude that the theory of animal origin is grounded upon insufficient evidence, and that the agent which produces the local lesion is non-pyogenic, and that suppuration, if it does occur, is probably due to secondary infection. They regard Parinaud's suggestion of foot-and-mouth disease as the source of the infection as purely hypothetical, although they mention as a rather striking fact that Parinaud's conjunctivitis has been reported only in France and America, countries in which foot-and-mouth disease is especially prevalent. They state that, moreover, five of the American cases occurred in cattle-raising sections, and one in Boston, a seaport from which cattle are exported in great numbers. The case reported by them gave no history of animal contact, but foot-and-mouth disease had recently made its appearance for the first time in years in the vicinity of the town in which the patient lived.

The pathological anatomy of the affection is also still in doubt. Gifford believes that the infection starts with the formation of small abscesses in or below the conjunctiva; that these abscesses break, a profuse discharge follows, and the granulations develop from



the edges of some of the ulcerations left by the abscesses. Verhoeff and Derby deny this, and believe that the primary lesion in this form of conjunctivitis is superficial, being confined almost exclusively to the subconjunctival tissue, and consists essentially in cell necrosis, followed by proliferation of connective tissue.

Treatment consists in antiseptic lotions and cauterization with silver or copper. When the granulations are large excision may be practised, and when the disease is very chronic and the swelling of the lids extreme and resistant, searing with the actual cautery may be necessitated. Alterative ointments should be applied to the affected glands, and if suppuration threatens, hot compresses, followed by incision and drainage.<sup>1</sup>

In the discussion following the reading of the paper the author stated that last winter he had had an opportunity of seeing a case of the disease, occurring in the practice of another oculist. *This case was also that of a physician whose right eye became affected in a manner typical of the form of conjunctivitis under discussion.* The swelling of the lids and the development of the polypoid granulation were, however, excessive, and the cornea became ulcerated, probably as a result of mechanical irritation. The course of the case was exceedingly chronic, as he understood that even now, a year after the initial symptoms had appeared, the granulations were still present.

He thought it of interest to note, in connection with the pathogenesis of Parinaud's conjunctivitis, that this case occurred in a physician who was a rectal specialist, that the first case occurred in a surgeon in hospital practice in Porto Rico, where the sanitary arrangements were most imperfect, and that the father of the child presented by Dr. Thomson was employed in handling fertilizer. Although bacteriological studies have failed to isolate the germ of this disease, he thought that the glandular involvement and the symptoms of general systemic depression all pointed to its being an infective process. He thought that the more frequent involvement of the right eye indicated that the toxic substance originating the inflammation was probably carried to the eye by the hand, and that, although bacteriological proof was wanting, he believed the coincidence of a possible source of animal infection to be present in too many cases, not to admit the probability of the disease being, as Parinaud first stated, originated in that way.

<sup>1</sup> Since the reading of this paper, the report of an additional case of Parinaud's conjunctivitis has appeared in the *Ophthalmic Review*, October, 1904, by Stirling and McCrae. Pure cultures of bacillus resembling Klebs-Loeffler bacillus were found, which led the authors to conclude that they were dealing with either a virulent form of bacillus *xerosis* or one less toxic than ordinary bacillus *diphtheriæ*.

A STUDY OF SIMULTANEOUS CONTRAST COLOR IMAGES.<sup>1</sup>

By CHARLES A. OLIVER, A.M., M.D.,  
OF PHILADELPHIA, PENNA., U. S. A.

IN December of 1901, while spending a number of most interesting and instructive evenings with Dr. S. Weir Mitchell, of this city, he called my attention to some curious visual phenomena which he had observed while gazing at some of the cascades in Japan; these phenomena consisted of a series of isolated, foam-like, and rapidly descending masses, showing a color display of brilliantly tinted lines, which fell and broke at corresponding depths with all the glow of prismatic scintillations.

We having determined from his individual knowledge that the conditions of the direct and the indirect natural illumination under which he had made his observations did not differ with the character of the light, except as to the degree of vividity and the peculiarities of color change, and, I being informed of the exact state of his rather rare form of autimctropia, opportunity was thus offered me to devise on these premises a number of apparatuses with which we experimented. Our results being so interesting, we repeated the studies in divers ways upon a number of scientific friends and acquaintances.

Through the kindness of a well-known firm of opticians in this city, a number of specially formed contrivances were constructed, which opened a new field of curious and unexpected results.

The experiments, which were conducted upon educated and observing men and women who possessed either normal uncorrected vision or normally corrected vision, all were made under similar though not identical conditions, which were noted in each instance. Nothing was suggested in any way to the subject, and everyone was allowed to express his sensations in his own way, by speech, writing, or drawing. Everything was voluntarily obtained; one eye was experimented upon at a time; the distance chosen for the testing was that which practically represented infinity; the apparatus employed was always placed in as near a true position for normal color reflection as was possible, and the time of day and the character and condition of the illuminants were considered in every case. All relevant facts were noted.

In two years from the time of the inception of the plan more than 1000 experiments were conducted upon some 600 subjects. Most of the trials were made by using rapidly moving bands of black and white. Control tests were made upon a number of subjects possess-

<sup>1</sup> Read before the Section on Ophthalmology of the College of Physicians of Philadelphia.

ing known degrees, both of congenital and acquired subnormal color perception.

After the performance of all of these experiments, methodical search was made throughout a large number of articles, monographs, and books upon the physiology of color, in order to find whether subjective contrast colors had ever been evolved in the same manner as that in which it had now been accomplished, and whether similar reasons had been deduced for the appearance of the phenomena.

With the exception of Francis Hopkinson's "Optical Problem Proposed to Mr. Rittenhouse and Solved by Him" in this city in the year 1785; Moigno's remarkably interesting and similar experiments; the unexplained results of the evolution of color fringes in Pear's (Barrett's) top of graded black and white concentric bands, and Bidwell's color phenomena, and the crude notes of such results in some of the ophthalmic text-books, several special monographs and journal articles, and the most interesting paper of Rivers "On Erythropsia," nothing was found which could be considered as more than explanatory of some pet theory or a conclusion drawn from doubtful premises.

The data obtained are summarized in the following statements:

1. Simultaneous color contrasts may be obtained through healthy visual apparatuses by the sudden repetition of imperfectly perceived areas of white.

2. The first contrasts noticed from fixed forms of white on black consist in constantly changing and irregularly grouped areas of uncertain "salmon reds," which assume varying tints dependent upon the shape, the degree of movement, and the relative sizes of the moving objects.

3. The secondary contrasts are fully complementary in values to the primary subjective "reddish" colorations, and consist of evanescent green borders, flecks, and bands, which appear alongside of the white objects, in front of the red subjectivisms, and on deeper and apparently farther-removed planes of vision.

4. When the objective "whites and blacks" are more ephemerally perceived, both the "red" and "green" subjectives appear simultaneously in connective bands, stripes, arrows, wedges, and all manner of anomalous forms, dependent upon the shape of the objects exposed, the rapidity of their movements, and the character of the individual visual apparatus.

5. All of these subjective manifestations are preceded by a brief impression of grayish or smoky areas, varying in intensity and momentarily projected and depressed.

6. In many cases, after and even during the appearance of the green-red complements, numerous blue-yellow tints appear in definite complementary relationships, some especially in the peripheral portions of the field.

7. Many of the higher-grade observers reported a number of the secondary and even tertiary color combinations which were usually seen as fleeting spots and stripes, these results obtained in addition to the phenomena of the ordinary color fatigue compressions.

8. Cases of subnormal color perception reduced in the ordinarily understood recognition of green, failed to evolve any properly tinted "green," as was shown by having these subjects select the tints they had seen from carefully chosen color-test wools. Neither did these cases obtain subjective expressions of the complement "red."

9. Cases of subnormal color perception lowered beyond that of the ordinary recognition of green and red, invariably reported "misty appearances," "grayish clouds," etc., followed by blue-yellow complements, but never noted any "green" and "red."

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## OBSERVATIONS OF A CASE OF BITEMPORAL HEMIANOPSIA WITH SOME UNUSUAL CHANGES IN THE VISUAL FIELDS.<sup>1</sup>

BY CLARENCE A. VEASEY, M.D.,

OF PHILADELPHIA,

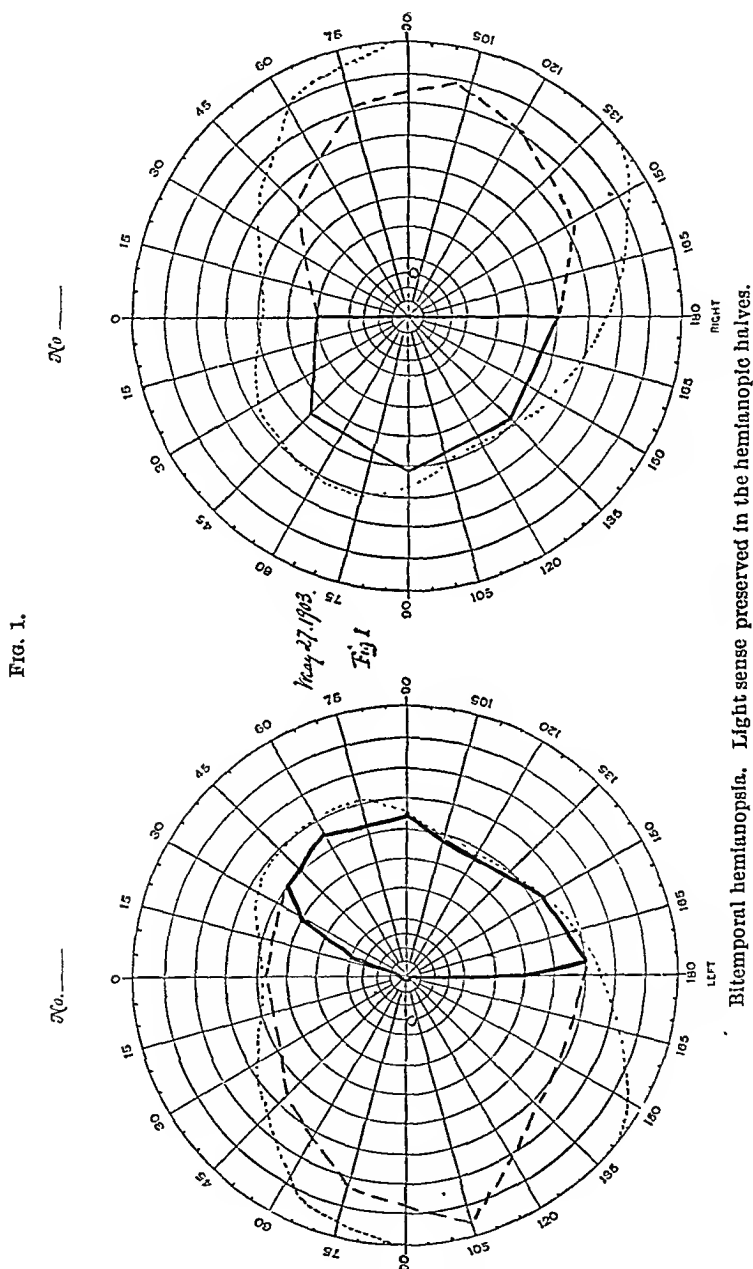
OPHTHALMIC SURGEON TO THE METHODIST EPISCOPAL HOSPITAL; ASSISTANT OPHTHALMIC SURGEON AND CHIEF OF CLINIC TO THE JEFFERSON MEDICAL COLLEGE HOSPITAL, ETC.

THE following case of bitemporal hemianopsia has seemed to the writer to present some unusual features of sufficient interest to merit its isolated report.

G. P. S., a married travelling salesman, aged thirty-four years, consulted me first on May 27, 1903, and presented the following history: His general health had always been excellent, and his appearance so indicated, as he was about six feet in height and weighed about 170 pounds. There was no history of any ocular trouble in his family, and though he began to wear glasses at sixteen years of age, for a low compound hyperopic astigmatism, his eyes had given him no trouble except the headaches which the glasses had corrected. Early in January, or six months before I first saw him, there had gradually appeared a "fogginess" of the temporal half of each field of vision, which he thinks was noticeable in the right eye before it was observed in the left. He placed himself under the care of a homœopathic oculist, who gave him as much as 50 grains of iodide of potassium three times a day, and this dose he had been taking for some months. Specific history was denied, and there were no other symptoms to cause its presence to be suspected. The urinary and blood examinations were negative.

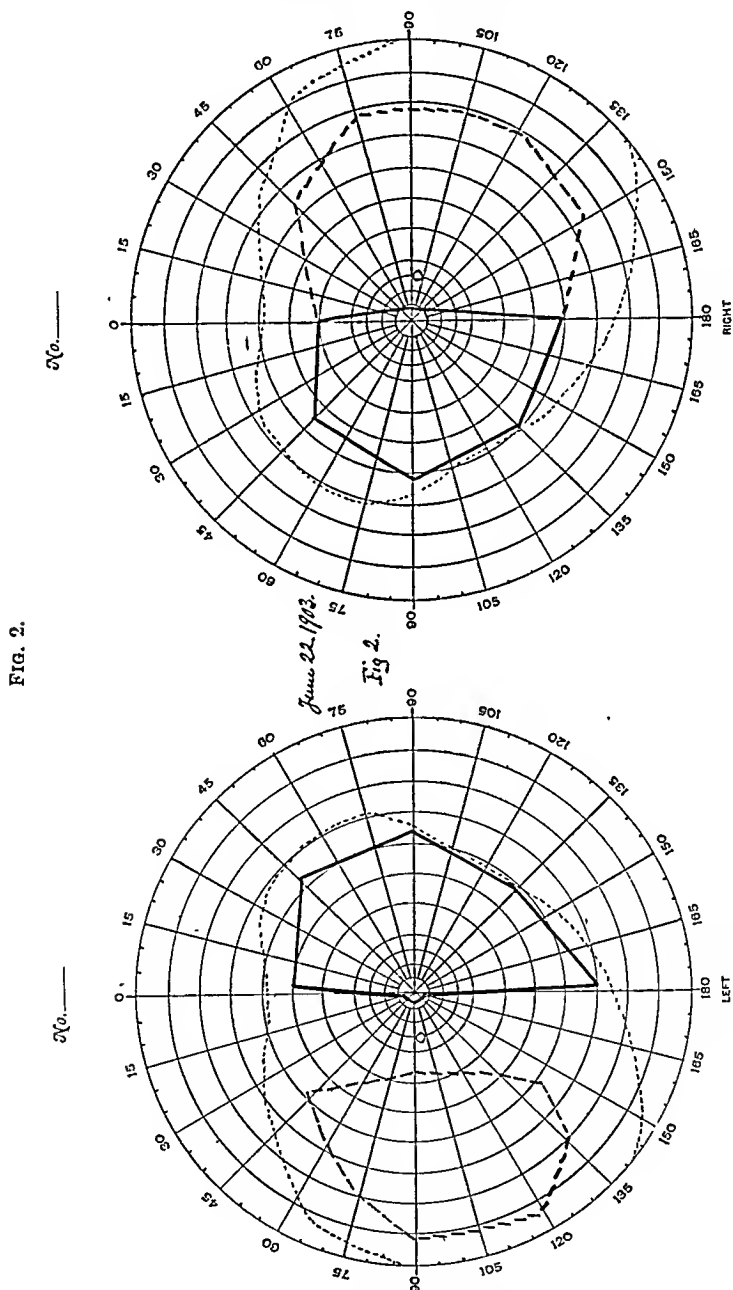
<sup>1</sup> Read at the Fortieth Annual Meeting of the American Ophthalmological Society, July, 1904.

Ophthalmoscopically, all the fundus details were normal, and have continued so to the present time. There is no blurring of the disk edges nor pallor of the nerve heads in any part. The fields of vision taken at the time of my first examination (May 27, 1903)



showed bitemporal hemianopsia, with the light sense still preserved in the hemianopic halves (Fig. 1). The dividing line was vertical in the right eye and passed directly through the fixation point, the patient stating that the round ivory disk in the centre

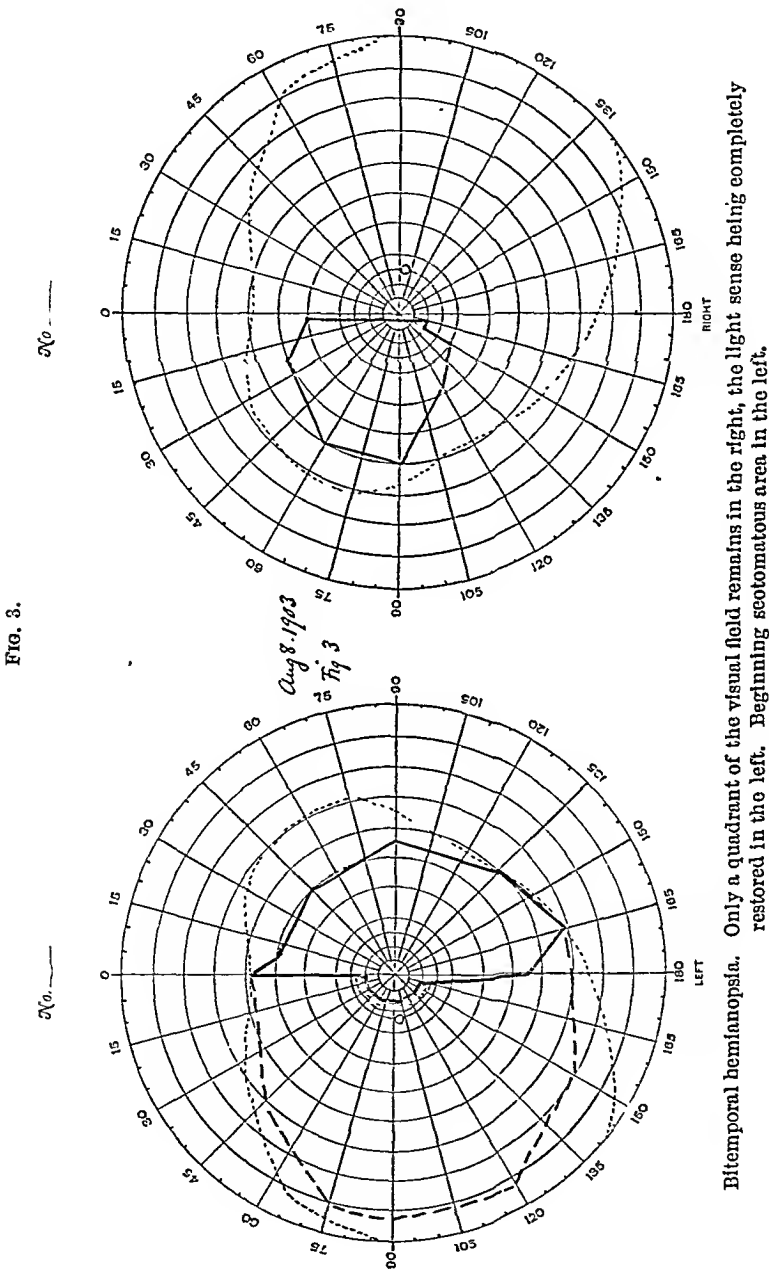
of the perimetric arc appeared as a semicircle. In the left eye the dividing line was inclined slightly to the right in the upper portion, and the fixation point was included in the preserved half of the field. Vision equalled 6/30, eccentrically, in the right and 6/15 in the left eye, but with both eyes 6/7.5 could be read slowly.



Bitemporal hemianopsia. Light sense in the hemianopic half of the left eye much reduced in area.

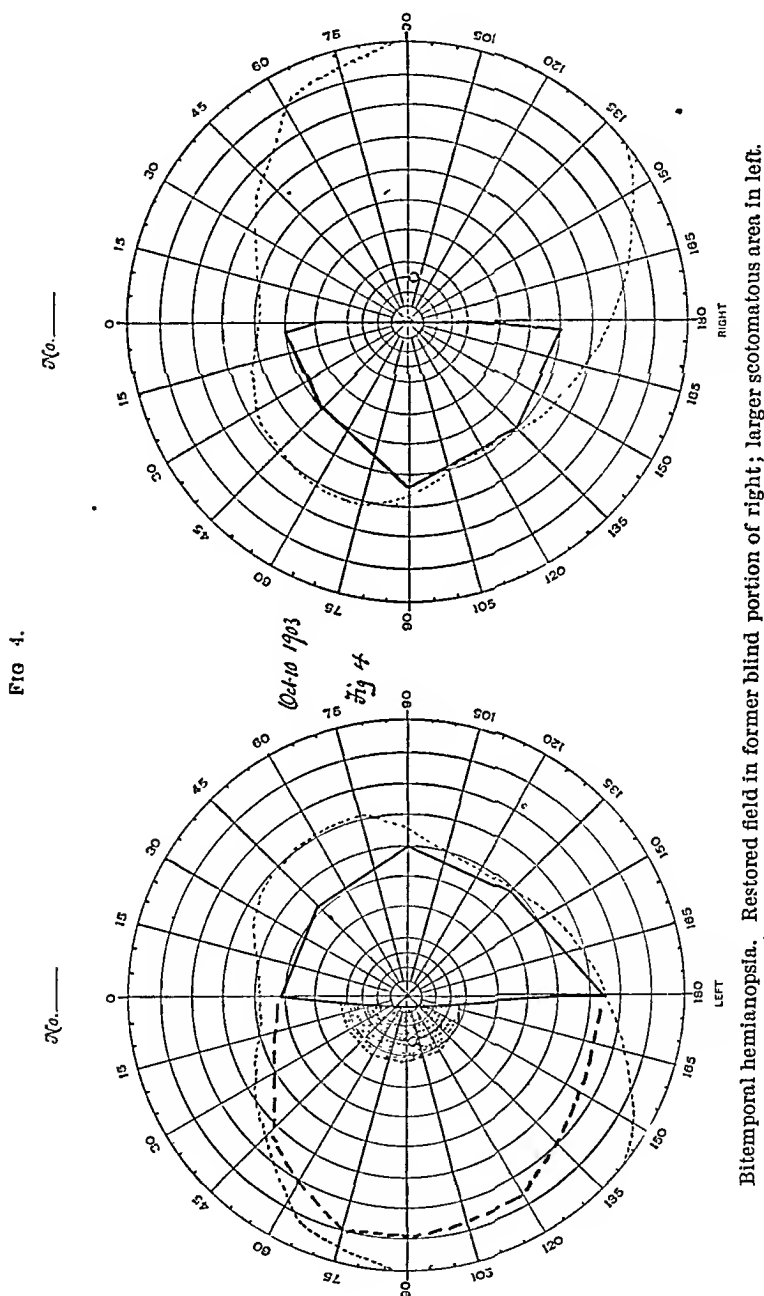
The visual fields, taken at frequent intervals, continued in practically the same condition until June 19th, a period of a little more than three weeks. On this date there was absolute hemianopsia in the right eye, the dividing line passing slightly to the right of

the fixation point, the light sense being still preserved in the left. On June 22d the light sense had returned in the former blind portion of the right eye, and the dividing line passed nearly 5 degrees to the right of the fixation point, affording normal visual acuity. In the



left eye the light sense was preserved only in the outer half of the temporal field (Fig. 2). During inhalation of amyl nitrite the fields cleared greatly, the patient being able to count fingers, distinguish objects (lead-pencil, bottle, hand, etc.) in the portion of

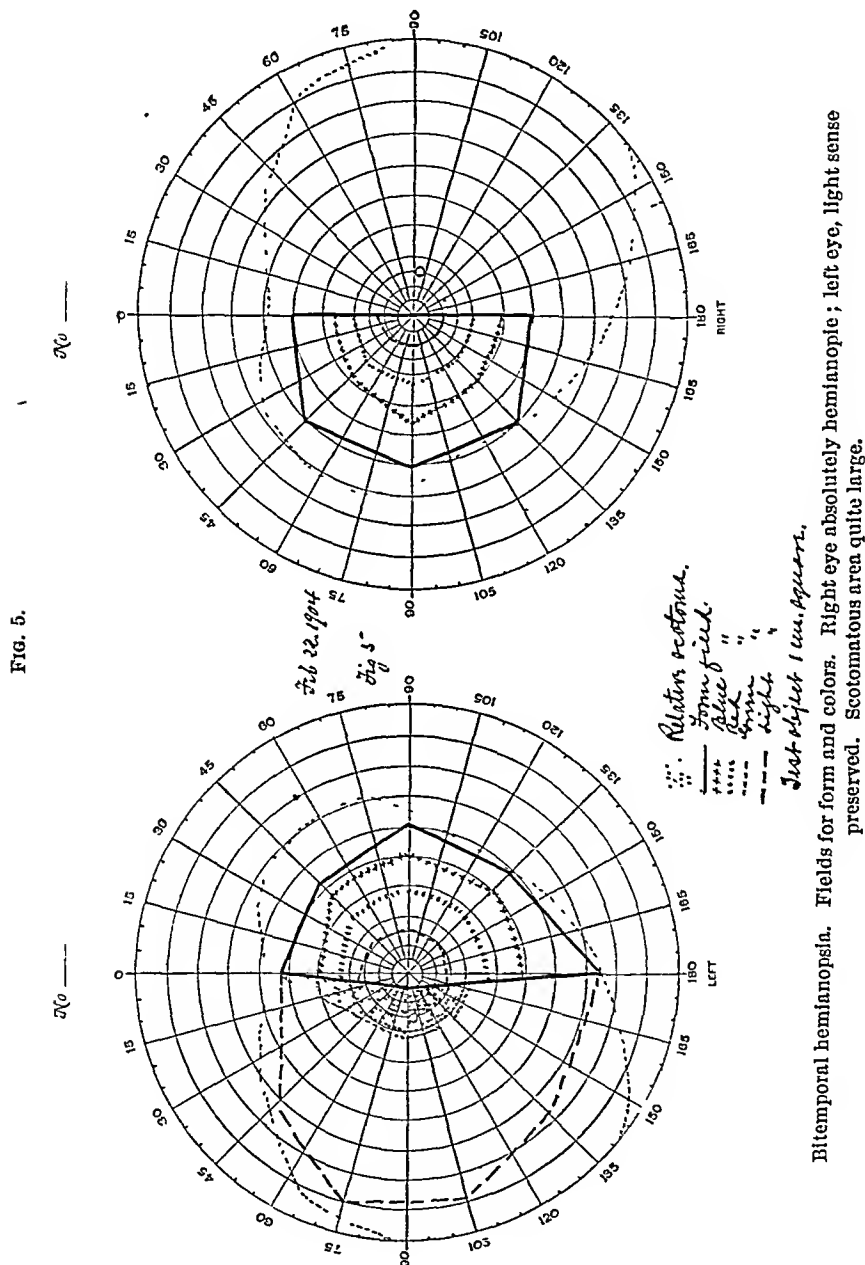
the fields in which the light sense was preserved, though the "foggi-ness" remained. On July 11th the temporal field of the right eye was absolutely hemianopic, the fixation point now being in the blind field, and in the left the light field was still preserved.



On August 8th there was found a very great change. In the right eye only the upper inner quadrant of the field was preserved, the remainder having lost all visual sense, and the dividing line passed about 2 degrees to the left of the median line and fixation point.



In the left eye light perception was still preserved in the outer field, but the dividing line now passed about 10 degrees to the left of the fixation point, and beyond this was an area 3 degrees wide in which form and color could be distinguished, though hazy; in

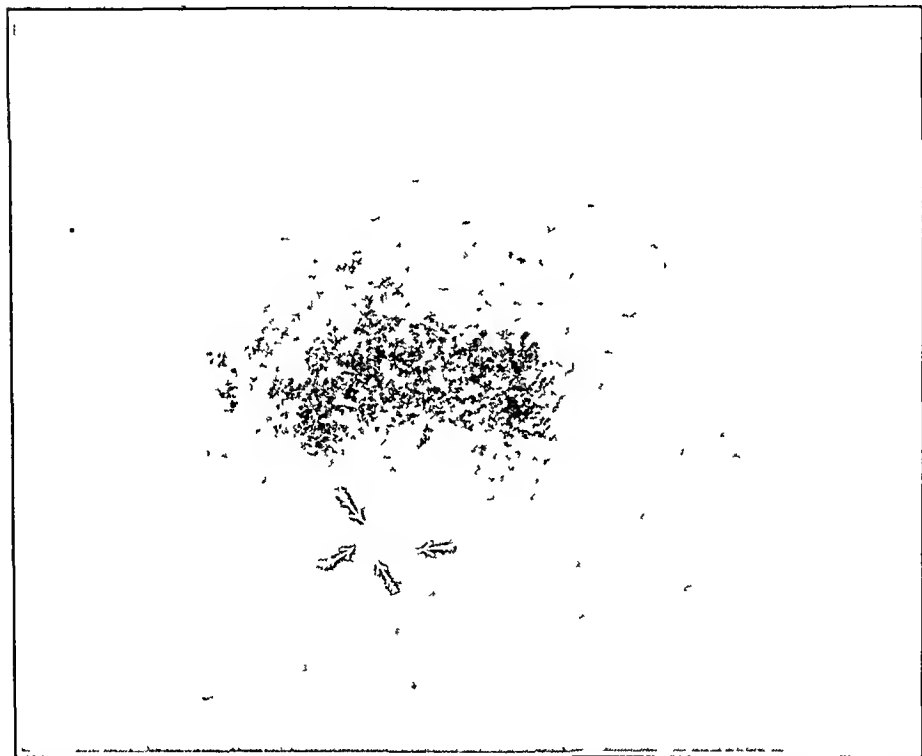


other words, the area was relatively scotomatous (Fig. 3). Vision in the right eye now equalled 3/100 eccentrically; in the left 6/6.

On October 10th the lower quadrant of the right field that had been lost at the time of the last examination was entirely restored.

The dividing line passed through the fixation point and vision equalled 6/22.3, slightly eccentrically. Vision in the temporal half remained totally abolished. The field of the left eye showed form perception in a larger area than before, light perception being still preserved in the outer half (Fig. 4). Since this time, a period of nine months, there has been but little variation in the character of the fields at any examination. At the present time about the only change from the examination just described is that the relative scotoma in the left eye is slightly larger, meaning restored vision

FIG. 6.



Skiagraph of brain showing shadow in region of chiasm. The half-tone reproduction does not show the shadows of the anterior choroid processes, though the latter are very distinct in the print and negative.

in a larger portion of the former blind field. The light sense is still present in the left, but lost in the right temporal field (Fig. 5). The vision in the right eye is 6/12, eccentrically, and in the left 6/6.

A skiagraphic examination of the brain of this patient shows a distinct shadow in the region of the chiasm. In presenting this skiagraph I fully realize the skepticism regarding skiagraphy of cerebral lesions, even when of large size, and the method has certainly proved of very little value thus far, except in furnishing corroborative evidence in those cases in which the diagnosis and the location had been previously determined by other means. In

the skiagraph (Fig. 6) herewith presented, however, it is possible, if it be held about a metre distant from the eyes, and in such a position that the light will be reflected from its surface, to observe distinctly a shadow in the area indicated by the arrows, and concerning which the skiagrapher, Dr. G. E. Pfahler, of Philadelphia, who has had a large experience in this line of work, writes as follows:

"The x-ray examination of the head of Mr. G. P. S., made January 23, 1904, shows a small and rather faint shadow, which is denser than the surrounding brain tissue, lying five-eighths of an inch above the floor of the sella turcica. This shadow is one-half inch in length and three-eighths of an inch in height. A tumor of this size lying at the middle of the brain could not be expected to cast a more dense shadow than that which is obtained in this skiagraph. The detail is always a little more clearly shown in the negative than in the print.

"In addition to the above, the anterior clinoid processes are about twice the length of the shadows obtained in any other head that I have examined."

In the line of treatment the patient has received almost everything that suggests itself in this class of cases. Mercurial inunctions, large doses of potassium iodide, pilocarpine sweats, salicylate of sodium, and thyroid extract have all been tried, but without appreciable effect.

As to the etiology, there is probably a small tumor in front of the chiasm, of a more or less vascular nature, that changes its size and thereby the amount of pressure from time to time, thus producing the alterations of the visual fields as described, the pressure not being sufficient to produce atrophic changes in the nerve heads. There is no history, nor any indication, of syphilis, and hysteria can be absolutely eliminated. Whether the lesion is an aneurysm of an anomalous artery, as in the case of Weir Mitchell and Dercum, or a solid vascular tumor, it is impossible to say; but it has been observed frequently during the treatment of the case that the fields were always worse in damp, cloudy weather, though the patient is only vaguely rheumatic, and he himself has frequently remarked that the fogginess seemed to be less dense when he was under the influence of antirheumatic remedies.

TYPHOIDAL INSANITY IN CHILDHOOD, WITH SOME  
NOTES AS TO ITS CHARACTER AND PROGNOSIS.<sup>1</sup>BY DAVID L. EDSALL, M.D.,  
OF PHILADELPHIA.

IF one wishes to base his prognosis in typhoidal insanity upon the views expressed by authorities, a glance at the writings of various medical clinicians and alienists is sufficient to show the confusing choice that is offered. As a rule medical clinicians look for a favorable outcome and extremely few admit that the mental derangement is likely to persist in as many as 20 per cent. of the cases. Alienists, on the contrary, state in most instances that a noteworthy percentage of cases remains insane. While a very small number of alienists consider that as few as 10 per cent. do not recover, figures approaching 33 per cent. are much more commonly given, and at the extreme of unfavorable prognoses one finds the opinion of so distinguished an authority as Clouston, who makes the startling statement that this form of mental disorder is rarely recovered from.

This diversity of opinion is found in regard to typhoidal insanity in children as well as in adults. Osler, for example, says emphatically in this connection that except for hemiplegia one need have no worry about the outcome of the post-infectious cerebral disturbances of childhood, since the subjects all recover. Holt refers to the condition only casually; Rotch, I think, not at all. Disquieting views are, however, expressed by a number of alienists who have specially discussed this question, and after reading such articles as that of Reddon there seems even to be a grain of truth in the saying of the French folk that a child that has typhoid fever either dies or becomes idiotic (Deroy). One very important explanation of these differences in opinion may readily be found. Medical clinicians, particularly medical consultants, see chiefly those cases that are of mild form and soon recover. Severe cases, or those that do not quickly improve, are generally seen from the beginning by alienists or fall into their hands after a short time. It is difficult, therefore, for either of these classes of practitioners to form a correct opinion of the course of the cases. One would anticipate that the truth lies at some point between the two extreme views, and probably nearer that of the general practitioner than that of the alienist, for the former has greater opportunity of seeing, at least temporarily, cases of varied severity.

I have made an attempt to determine by a search of the literature what the outcome of typhoidal insanity is likely to be when the

<sup>1</sup> Read by invitation at the meeting of the Medico-Chirurgical Faculty, Baltimore, May 20, 1904.

condition occurs in children, what influence the nature of the mental disturbance should have on the prognosis (a point that is naturally of much importance but that has been largely neglected by systematic writers on children's diseases), and the influence of heredity on the incidence and the outcome. I have also attempted to get a general idea as to the frequency of the condition and as to some minor points, such as age and sex. In making these statistics I have not attempted to collect all the cases on record, as I can see no usefulness in such a plan in this instance. I have simply gathered together a group of cases large enough to be probably somewhat representative, and have tried to collect cases from varied sources, that is, cases reported by general clinicians and pediatricists as well as by alienists. The classification that I have used has been made as simple as possible, including only mania, melancholia, dementia, chronic paranoia, and a group of simple deliriums of convalescence, these latter cases showing marked though only temporary delusions or hallucinations with no other psychic disorder. The grouping of the individual cases has in many instances been very difficult, partly because it has been done by a medical clinician whose knowledge of questions in alienism is crude, partly because of the general disorder that has existed among alienists for years past in regard to the classification of insanities, and most largely because many of the cases were found mentioned only very casually by those reporting them, and some cases have necessarily been taken from abstracts. In a considerable number of instances the same cases have been found briefly mentioned a number of times by the observers or their students, and the classification of these cases has been determined by combining the facts given in various places. On the whole I trust that the grouping is fairly correct, and I think any errors would have little influence upon the conclusions that I shall draw.

The points that are brought out by the study of these cases are, in some instances, very striking and important. They are chiefly the following: In the first place it was exceedingly easy to find over 80 cases mentioned in the literature, though in many instances the search for the original source of these cases was difficult. The readiness, however, with which cases may be found in the literature, together with the fact that I have learned in casual conversation with a considerable number of practitioners that they have seen cases of this condition, convinces me that the statement commonly made by modern alienists that typhoidal insanity in childhood is not rare, is more nearly correct than the statement made by a large proportion of medical clinicians or pediatricists when these latter mention the condition at all. I have seen two cases in children in which there was distinct insanity, one of which I shall describe in detail later; and at a meeting of the Philadelphia Pediatric Society, when an abstract of this paper was read, there were present five

persons in general practice who had seen from one to three cases. There can be no doubt, I think, that while it is uncommon it is not extremely rare.

The figures that I have obtained as to the nature of the insanity are very striking and in some ways unexpected. They show 36 manias, 26 dementias, 6 melancholias, 14 instances of delirium of convalescence with simple delusions or hallucinations, 1 chronic paranoia. As I said, the cases have been difficult to group. I may, for example, have put a certain number of almost pure melancholias among the manias or dementias, for I included cases under mania whenever the reports showed a distinct tendency to violence or to excitement of a form that was not dependent merely upon the fearful delusions of melancholia, even when this tendency was but brief. I classed as dementia those cases in which the chief symptoms were stupidity and loss of intellectual acquirements. These cases, of course, sometimes showed a tendency to violence and more or less severe excitement. Some of them were of mild form and apparently of brief duration, and I doubt whether more detailed descriptions would have permitted of classifying all of them as actual dementias or as anything more than a mere temporary stupidity of marked degree dependent upon exhaustion. I have, however, as far as possible excluded cases in which there was no evidence of actual mental derangement. I may have included under this group too many of the milder and briefer cases, but exclusion of them would have made the already very unfavorable figures as to the outcome of dementia still more strikingly unfavorable.

The small figure for melancholia, only 6 cases being so classed, is certainly not representative and does not give a clear idea of the conditions that one actually meets. A large proportion of the cases of mania show a very pronounced element of melancholia, but when there was any maniacal tendency I have grouped them under mania.

The figures concerning the outcome of cases are as follows: Excluding the simple deliriums of convalescence, all of which recovered and which are clearly of a type that may be separated from the other cases, there was a total of 69 cases. Of these 43, or 62.3 per cent., recovered; 23, or 33.33 per cent., remained insane; 3, or 4.34 per cent., died. Of the manias, 29 recovered, 2 died, and in 5 insanity persisted; that is, 5.55 per cent. died; 13.89 per cent. remained insane. Of the dementias, 9 recovered, 1 died (during the acuteness of the attack, but apparently from erysipelas), and 16 remained demented; in other words, 3.8 per cent. died and 61.61 per cent. were persistently demented. Of the 6 melancholias, 5 recovered and 1 remained subject to severe melancholia after many years; that is, in 16.66 per cent. the condition persisted. The figures for melancholia are, of course, too small to represent the facts properly.

So far as these figures may be followed, then, they apparently demonstrate two important points. The first is that the percentage of cases in which insanity persisted is much nearer to the figures given by many alienists than it is to the statements of most medical clinicians or pediatricists. These statistics, therefore, throw a rather gloomy light upon the outcome. The most striking point, however, and the one that seems to me most important, is the influence of the character of the insanity upon the outcome. This will not surprise anyone at all acquainted with questions in alienism, but it is a point that is little if at all referred to in this connection by anyone but alienists. Dementias are, as might naturally be expected, of far graver prognosis when of marked degree than are the other forms of insanity. The simple delusions and hallucinations without other mental disturbance seem practically always to get well.

After mentioning these figures I would, however, at once state that I do not consider that they can be wholly believed and accepted as representative of actual conditions. In the first place it is perfectly evident that the more marked cases of this condition are likely to be reported, while the milder cases are not, both because the milder cases make less striking reports and because they are often overlooked. Also, the figures that I have given have necessarily been more largely drawn from the experience of alienists than from that of general clinicians, since it has been impossible to avoid this entirely. I believe that the condition is much more common than the number of cases I have collected would indicate, and I believe, also, that it is frequently overlooked, and that the cases that are overlooked or not reported are chiefly the milder ones. Hence, I believe the prognosis is much better than these figures would indicate. On the other hand, the fact that a considerable number of cases in which the insanity persists could readily be found in the literature shows, to my mind, quite clearly that the condition is one of greater gravity than is commonly believed or is taught by others than alienists; and I am sure that the figures also show, as is wholly to be expected, that the form of insanity is of great importance in establishing a prognosis.

As to the influence of heredity, I have not followed this point out in all the cases, for important as it is, the question of heredity is so infrequently mentioned by either medical clinicians or alienists that I am convinced that any figures obtained from the entire series of cases would not represent facts. The figures that I have obtained, however, are surprising. One would naturally expect to find heredity frequently influential in producing this condition, and particularly in causing its persistence. So far as I have gone I have found among the manias the question of heredity mentioned nine times; in each instance, it happens, in cases that recovered. Five of these had good family histories, in two instances a number of children of the same generation had died of convulsions, in two

there was alcoholism in the parents. Among the dementias I have found seven instances in which heredity was mentioned. All these cases, it happens, persisted. In 5 cases the family history was wholly good, in 1 several brothers and sisters had died early of convulsions; in one the father was a man of general bad character. Of four instances among the melancholias in which there was mention of heredity three showed good family histories and one a history of young brothers and sisters dying of convulsions. The 1 case of paranoia showed a bad family history which included insanity, but in no other instance among the twenty that I have mentioned was there any note of insanity in the family; and, as was stated, the family history in thirteen out of twenty instances was entirely good. The surprising point is to find so little mention of insanity or other severe nervous conditions in the family and to find an almost entire lack of indication that heredity has any influence in causing persistence of the mental disorder. One can hardly believe that if this point had been accurately investigated by all those who observed the cases there would have been such a result in a collective study. The possible dreadful influence of a family tendency is shown by the observation of Morel who saw 8 cases in the children of one family, and 5 of these cases were persistent. Unfortunately, he does not give the mental history of the progenitors.

The important points, then, that are brought out by my study of the literature are that in an appreciable number of cases the insanity persists; that mania is but little more common than dementia, while melancholia is much less common, and that a very marked proportion of the dementias do not get well. Dementias following typhoid fever must be much more common in childhood than in adults; this is considered to be the case by a number of writers upon this subject.

I need make but brief reference to the questions of age, sex, and the period at which the insanity developed. The facts concerning the ages of the patients are those of chief interest. I have divided them into three groups as follows: So far as I have notes of the ages there were from two and one-half to five years of age 14 cases; from six to ten years of age there were 26 cases; from eleven to fifteen years of age there were 27 cases. The number that occurred in the first few years of life is striking and especially noteworthy, as is also the fact that practically the same number occurred between six and ten years as between ten and fifteen years. It is repeatedly stated in the literature concerning this question that mental derangements are much more common in the late years of childhood than earlier. This is not borne out by these figures. As to sex there is nothing of great importance. The notes that I have concerning this point show thirty-nine boys and twenty-five girls; the only fact of interest being that I find in my notes under mania three times as many boys as girls, the boys numbering twenty-one the girls seven. This differ-



ence may be largely due to chance. As to the time of occurrence of the insanity in relation to the attack of typhoid fever I have notes on this point in 65 cases. In 54 of these the symptoms of mental derangement are said to have arisen in convalescence; in 11 during the course of the disease. I lay no weight upon these figures. In some of the cases the description of the course as given by the author shows that distinct symptoms of insanity arose in the course of the disease, and yet the period of the development of the insanity is put down as convalescence. I am convinced that a larger proportion of cases of infectious insanities than is usually stated show distinct evidence of actual insanity before convalescence begins. This is largely a question of the care with which the cases have been previously observed. Delirium is so common that very often relatively little attention is paid to its character, and yet the character of the delirium is frequently sufficient warning of the probable appearance of a definite psychosis or of its actual presence. I have, in all, seen 8 cases of typhoidal insanity. In one case, which was one of dementia in an adult, it was I think impossible to make out during the course of the disease that there was any other mental disturbance than profound hebetude. In 6 other cases, however, there were present during the late course of the disease either persistent and well-marked delusions, usually of persecution, or a profoundly melancholic condition; and while in several instances marked symptoms of an actual psychosis did not develop until convalescence was well established, a distinct psychosis was thought to be present in all these cases before convalescence began. The eighth case was a rapidly fatal instance of Bell's mania that occurred during the course of a very mild typhoid fever.

It is almost impossible to make any satisfactory statement as to the actual frequency of typhoidal insanity in childhood. Deroy says that it occurs about once in 200 cases. I am unable to determine how he reaches this conclusion, as the literature I have gone over does not permit of a well-founded decision upon this point. It would be interesting to determine the frequency of the condition in childhood as compared with adult life, but this also is a very difficult point to settle. On the whole, judging from individual expressions of general clinicians and alienists, one gains the impression that it is little if at all less common in children than in adults.

As is the case with other forms of insanity, it is very often much more difficult to determine with children that typhoidal insanity is present and when it began than it is with adults. One reason for this is, of course, the difficulty of gaining the confidence of children, particularly when they are quite young, and of persuading them to talk freely. Another difficulty is that most children have less self-control than adults, and it is more difficult to determine to what extent any loss of self-control is pathological. Furthermore, many young children are extremely imaginative without being in

the least insane, and they may have well-formed and persistent delusions and hallucinations as a result of long-continued exercise of their imaginations; and yet their curious ideas, which are sometimes very disturbing, practically always disappear spontaneously without being accompanied or followed by a trace of actual mental disorder. With an imaginative child, therefore, it is somewhat difficult, particularly when such a child is convalescing from a grave disease, to determine the importance of delusions and hallucinations; and such conditions, therefore, when entirely unaccompanied by other mental disturbance belong in a separate class in childhood even more distinctively than they do in adult life. It is also at times difficult to determine whether a child has actual melancholia, especially if it is in a hospital, or whether any severe mental depression present is due to marked homesickness, to longing for food, or to other causes of emotional disturbance that would be much less active in adults. I make these observations in order to dwell with some emphasis upon the fact that certain conditions that are not distinctly pathological are even more difficult to distinguish from actual mental disorder in childhood than in adult life. Most practitioners I think neglect early consideration of the possible presence of mental disorder in a child and attribute the conditions present to mere peevishness, homesickness, hunger, or ill temper, unless the symptoms become so severe that it is easy to see that the child is not sane. This is a matter of real importance, because it is, of course, in the early stages of these mental derangements, particularly when they are not toxic but nutritional in origin, that treatment can be most successfully instituted and the services of an alienist should be secured at that time. I have recently in two cases seen post-infectious insanity in childhood that was clearly marked, and soon indeed became perfectly evident, but that had been overlooked by the attendants and the child's mental state had been attributed to peevishness and ill temper. At the time I saw these children it would have been more proper to have called in an alienist.

I will mention but a few facts concerning the character of the mental disturbance in these cases and then describe briefly a case of my own seen some years ago; and, at somewhat greater length, a more recent case. Those who wish a systematic description of the condition may find it in the works of alienists such as Moreau de Tours or Emminghaus or in one of the several French theses referring to this subject, for example, those of Deroy, Dieuzaide, and Reddon. The conditions observed are not very different from those in other post-infectious insanities in adults or children.

The commonest form of insanity in these cases as shown by my figures is mania. There is in most of the manias a very pronounced element of melancholia, but this is interrupted by brief or longer periods of maniacal violence or excitement in which the children

tend to resist any attempt to control them, often cut, tear, or break any objects at hand, sometimes do deliberate violence to those near them, and at times are in a state of great exaltation. In some of the cases the melancholic element is entirely absent and there is a pure mania of exaltation, sometimes associated with a tendency to violence, sometimes not. These cases are, however, much less common than those with a decided element of depression. In a large proportion of the manias, and in most of the melancholias, there is a very pronounced degree of the confusional state that is so common in all post-infectious mental disorders in both adults and children. The children grow confused as to persons, place, time, etc., and this element often becomes so marked as to approach actual dementia. The lines distinguishing mania, melancholia, and dementia are indeed often extremely difficult to draw, particularly from the descriptions given in reporting cases. The dementias show marked weakness of intellect rather than confusion, and are frequently dirty in their habits. The melancholias that show no tendency to maniacal outbreaks are few in number as is indicated by the figures that have already been given. In these cases, as well as in those that show maniacal symptoms, there is usually the appearance of profound unhappiness, often delusions of persecution, or extreme oversensitiveness, frequently loud and persistent complaints of unhappiness or of ill treatment, with at times fearful delusions and hallucinations.

As examples of the deliriums of convalescence I may mention the case of Thoré in which the child had a delusion for sometime that both legs had been cut off; another case (Hanot) in which the child had a delusion that he had two watches, one gold and one silver; another child (Simon) had a delusion that a coach and four was waiting for him outside the house. The delusions are most commonly delusions of grandeur; the hallucinations are often terrifying.

As an example of a simple acute dementia I will mention a case of my own that occurred six years ago in my service at St. Christopher's Hospital, in a boy four years old. I am not absolutely certain that the child had typhoid fever, but he had a long febrile attack for which I could find no other cause, and he gave a Widal reaction. The attack was not very severe, but during convalescence the child was stupid, exercised no control over his urine or feces, and paid practically no attention to anybody or anything about the ward. It was necessary to urge him to eat. When he was sitting up or was allowed to go about the ward he made no effort to amuse himself in any way and showed no interest in the other children or, so far as could be determined, in anything. He had no appearance of melancholia. He seemed to have lost memory, speech, and most of the other intellectual acquirements of a child of that age. This condition persisted for nearly seven weeks after convalescence had begun and he then began gradually to recover and a few weeks

afterward was discharged almost entirely well. So far as we could learn he ultimately became perfectly normal.

A case that is a very representative example of the commonest form of typhoidal mental disturbance in childhood, that in which there is a mixture of mental confusion, melancholia, and occasional maniacal outbreaks, was observed in my service at the Episcopal Hospital last spring. The child, who was a girl nine years of age, was admitted on the 9th of March to the children's ward, and during the course of the fever was under the care of Dr. D. J. Milton Miller. Her family history included a number of instances of phthisis in members of the mother's family. There was a history of nervous disturbance in the mother; she had for years been subject to periods of marked depression which had never been considered insanity but which, from the husband's description, were probably mild melancholia. One sister of the patient had died of phthisis. The family history was otherwise negative. The child's previous personal history included whooping-cough, mumps, and diphtheria. She had when admitted characteristic signs of typhoid fever and passed through a very severe attack. From the early part of the attack throughout the whole illness she had marked nervous symptoms; she was at first extremely apathetic and moaned a great deal, and afterward developed so much irritability, rigidity, and other signs suggesting meningitis that lumbar puncture was twice done but no fluid was secured either time. When I went on duty on April 1, 1904, Dr. Miller directed my attention to the very marked nervous symptoms that the child exhibited. Fever had been absent since the 28th of March, but she lay in bed moaning, calling for her mother, begging for food, and fretting almost continuously. She had, during the fever, had for some time the distinct delusion that her mother was dead. This idea had disappeared and at the time I first saw her she presented no mental symptoms except the conditions that I have mentioned. She had an enormous appetite, and begged for food most of the time, although she was fed as freely as possible, and even later on when she got semisolid or solid food in large quantities she would eat a very large meal and immediately wail for more food. She had become very much emaciated, was pale, her extremities were cold, the pulse small and weak, the peripheral circulation sluggish. The physical signs were otherwise normal excepting for some weakness of the heart sounds. The patient slept well at night, but refused to rest during the day, and it was impossible to keep her at rest for any length of time without using force.

After a few days it was noticed that she was developing more signs of a psychosis, and within the next week the following facts were noted: Part of the time she was merely extremely dejected in appearance and was entirely quiet, but she often showed extreme fearfulness at the most trivial occurrence, such as the arrival of a nurse or a doctor in the ward, or any sudden movement near her or

attempt to examine her. She frequently cried out with a sudden, distressed wail, sometimes short, sometimes prolonged and intensely shrill. She expressed fear of almost every person and was afraid that everyone was about to do her physical injury or to say disagreeable things to her; but she would go to anyone, even a stranger, almost at once, and she often threw herself wailing into the arms of the nurses or doctors as if for protection. Her expressions of fear and of other emotions were, however, entirely irrelevant to her actions; for instance, she would suddenly in the midst of a conversation sing a few lines of a comic song, tapping her feet or dancing at the same time, but maintaining a most dejected look and usually ending her jolly song with a wail. Dr. Burr kindly saw her with me at this time.

It was determined that she had a number of hallucinations of hearing; for example, she believed that an angel came to her bed and talked with her every night. She had also very frequent hallucinations of sight, exclaiming, "There is that darkey," "There is my uncle," etc. She frequently rushed to see some friend or relative who she believed was coming into the ward. She also persisted much of the time in stating that Dr. Moncure, my resident physician, was her uncle, of whom she was very fond, and she constantly called upon Dr. Moncure for protection and begged him not to go away from her; she knew her uncle, however, when he visited her, and she occasionally looked at Dr. Moncure and said in a disappointed tone, "That is not my Uncle Ed." At times she seemed to be afraid of Dr. Moncure and called him "That doctor," and said that he was going to hurt her. Sometimes she called her relatives by their correct names, frequently she called them by the names of other relatives. She could read, write, etc., recognized correctly all sorts of objects, and described their uses at all periods of her mental disturbance. She had marked religious emotion occasionally, and then recited many prayers over and over; and she often suddenly adopted the attitude of prayer. She had marked delusions of persecution, was exceedingly sensitive and suspicious, and believed that everybody was about to injure her or was calling her unpleasant names of various kinds; she also thought that we had all planned to cut off her leg, and this delusion persistently recurred. On April 15th she told me that Dr. Moncure had "threatened to cut her throat with a pen-knife." When asked if this were actually true she said "No," but that her father had said this, and she then persisted in the statement that he had frequently made such threats. Her father, however, was evidently very fond of her and she always appeared happier with him than at any other time. On April 17th, after this delusion had apparently been absent for a long time, she suddenly again insisted that her mother was dead and told a detailed story of her death on Christmas night after the birth of twins. She was at this time very much mixed as to time; for instance, she said at one moment that she had been in the hospital two years; again, that she had been there

only a few days. Within a few days she had a curious transformation from the first person to the third person in her manner of speaking of herself. She had constantly tended to cry out loudly "Oh, oh, oh!" and often ended with, "I am so unhappy, oh!" She ended every question or answer or any statement with a wail, but always spoke of herself in the first person. On April 19th she spoke of herself only in the second person, for example, she repeatedly said, "You, Marie, must die." On April 20th, and for a day or two thereafter, her personality had become so completely transformed that she insisted that Marie M. (her real self) was dead and that she was Marie Dougherty. She said that Marie M. had died because of her evil doings. She also had an evident suicidal tendency for several days at this period, often saying that she must die because she had been so bad, and the sooner she died the better; and she reflected upon the best ways of dying. She was more confused at this time than she had been, sometimes being unable to recall names of the nurses and the doctors, though she had known them before; she was also much more mixed as to time. She had likewise grown careless about her habits, and the nurse said she nearly always soiled her clothes unless taken regularly to the closet. She had no noteworthy tendency to violence excepting on April 22d and for a few days thereafter. On April 22d she attempted to tear up her bedclothes and fought violently when interfered with, and for a few days after this she tended to be violent when any attempt was made to restrain her, and she occasionally fought, bit, and scratched the nurses. Early on the morning of April 23d she got out of bed suddenly from apparent sleep and went rapidly into a private room next the ward, and when the occupant of that room tried to send her back to the ward she fought violently for a few moments and insisted that an angel was waiting for her in the room. This was perhaps partly dreaming and somnambulism, as the nurse stated that she seemed to realize suddenly where she was after a few moments had passed and then became entirely quiet; and next day the child gave me herself a clear account of this occurrence, and said she had been dreaming and showed the first actual amusement that she had exhibited since her admission. After this time she became less noisy and unhappy and at the end of a week she had improved greatly; and at that time she begged constantly that she might be taken home. I believed that her mental disturbance was being maintained by her homesickness and sent her home on May 3d; and after this she improved with the greatest rapidity. I saw her two weeks afterward at her home and at that time the only psychic abnormality that she exhibited was a tendency to sit by herself with an abstracted manner and to grow a little unhappy-looking; if diverted, however, she was jolly and happy and had no delusions or hallucinations. Four months afterwards she called upon Dr. Moncure at the hospital and was then and had been for some time perfectly well.

The course of this child's mental disturbance and that of almost all the other cases of typhoidal insanity that I have seen was directly related to the condition of the general nutrition. This is not a new statement, but one upon which alienists strongly insist; it is, however, a fact that I believe does not receive sufficient appreciation. A certain number of these cases are unquestionably toxic in their origin, and possibly almost all are toxic in their inception; but whether this is true or not, in nearly all of them there is a very large nutritional element. The histories of the cases show no consistent relation to the severity of the attack of typhoid fever; there is, however, with extreme frequency a story of very marked reduction of nutrition, and, as in my last case, the subjects, both children and adults, often have an enormous appetite and suffer most acutely from hunger. I think it is impossible to insist too strongly upon the importance of this in connection with typhoidal psychoses. Contrary to a somewhat widespread tendency that has been manifested for some years past, I have in most cases been constantly more inclined to restrict the diet of typhoid cases to milk almost exclusively, and I have also been inclined to restrict the amount rather than to increase it; but in cases that show any distinct tendency to the development of a psychosis, as, for example, in cases that have persistent delusions, especially during the latter part of the attack, I believe that the feeding should be as free as possible even during the latter part of the fever, and, particularly if suspicious symptoms remain present or develop, the food should be very rapidly increased during convalescence.

One point perhaps deserves very brief mention. It has been suggested by a number of French writers that typhoidal psychoses occur with especial frequency in certain epidemics, and it would be of interest to attempt to determine whether this is true. In the spring of 1904 I had, in a service in which there were, all told, about 50 cases of typhoid fever in four months, 5 cases of marked psychosis, one of them being the child last described, the others adults. This is, of course, a wholly abnormal percentage of cases. Their occurrence together may have been a mere coincidence; but it does not seem impossible that mental symptoms and complications may be much more common in certain epidemics, just as various other symptoms are more frequent at certain times than at others.

One other point seems to me to be of some importance in connection with children. Valuable as institutional treatment is in insanity, I think that when the cases are not wholly unsuited to it, treatment at home is often better for these children, particularly when they are very melancholy, as was my patient. There are numerous stories in the literature of this subject of the evidences of profound homesickness, and this is surely capable of increasing the psychosis and of causing its persistence for an undue period; and in the cases in which this was noted rapid improvement usually occurred after the patients were sent home. Home treatment is, of course, not

suitable for violent cases, and the home conditions as well as the individual patient need to be carefully considered in each case. But in mild cases, and especially in cases that are improving but remain depressed and homesick, treatment at home, or at least removal from the unnatural atmosphere of a hospital or other institution, has repeatedly given a rapid impetus toward recovery. This is, I think, more apt to be the case with children than with adults, and certainly the children of the poor are not less likely to be benefited by this measure than the children of the well-to-do.

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## REVIEWS.

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A TREATISE ON THE PRINCIPLES AND PRACTICE OF GYNECOLOGY.  
By E. C. DUDLEY, A.M., M.D. Fourth Edition. Philadelphia  
and New York: Lea Bros & Co.

DR. DUDLEY is well known as a sound teacher and this book bears added testimony to this reputation. We do not remember a work upon gynecology which we have read with greater pleasure. The mechanical part of the book is perfect, the illustrations are good, and with two exceptions serve to elucidate the text in an admirable manner. The exceptions noted are the depiction of a bladder calculus and a hairpin contained within the bladder, for neither of which can we see the use.

Among the best chapters of the book, though it is somewhat difficult to make a choice, are those dealing with Fibroid Tumors, Malignant Disease of the Uterus, and Extrauterine Pregnancy, one of the strongest points of the two former chapters being the consideration of the operative treatment, which is most carefully detailed and clearly illustrated by very striking full-page plates.

A chapter upon Embryology of the Genitalia and Congenital Malformations, also well illustrated, contains the salient points of the former necessary to the full understanding of the latter. The chapter upon Perineorrhaphy is excellent and will repay careful reading, the illustrations again being the result of most painstaking work upon the part of the artist as well as the author. We are glad to note that the immediate repair after labor of lacerations of the cervix is advised against. The whole subject of abnormalities of position of the uterus is considered at length and an operation for severe grades of procidentia, based upon the dictum of Reynolds that the bases of the broad ligaments as fixed points should be used to anchor the cervix in a backward direction, is illustrated and carefully explained.

We do not, however, agree with the author that the amputation of the cervix is rarely indicated in the treatment of uterine prolapse.

In dealing with the operative treatment of uterine retrodisplacements the operation known as Alexander's is given its proper place as being indicated in but relatively few cases; the author stating his preference for hysterorrhaphy, in all cases in which the abdomen is opened instead of for intra-abdominal shortening of the round

ligaments. In the performance of hysterorrhaphy he uses three sutures, all introduced on the posterior aspect of the womb; one being applied at each cornua and the other in the median portion of the organ.

We believe this to be a mistake in technique, as a better position—*i. e.*, one more nearly approaching the natural, is secured and less danger of subsequent dystocia is occasioned, by the introduction of the sutures into the top of the fundus in a line with the tubal ends.

These slight criticisms upon really unimportant matters are all that can be offered and the author is to be most heartily congratulated upon the production of a most useful text-book. W. R. N.

WEATHER INFLUENCES: AN EMPIRICAL STUDY OF THE MENTAL AND PHYSIOLOGICAL EFFECTS OF DEFINITE METEOROLOGICAL CONDITIONS. By EDWIN GRANT DEXTER, Ph.D., Professor of Education at the University of Illinois; with introduction by CLEVELAND ABBE, LL.D. New York: The Macmillan Company.

THE early part of this volume is devoted to an historical account of weather lore. Old sayings, weather prophecies, legends handed down from generation to generation are here recounted and quoted. Popular superstitions, past and present, concerning the relation of lower animals to the weather conditions, are brought before the reader in an interesting and entertaining manner. The author has evidently gone deeply into this subject of superstition and weather prophecy, and gives many examples from English and American sources. He also shows the effect of weather influence on the mind of authors and men of letters, quoting freely passages illustrative of the popular belief in weather signs and portents.

The greater and scientific portion of the book is devoted to statistical deductions pertaining to the effect of meteorological conditions on the moral deportment of mankind. The author has procured his data from officials of various schools, prisons, and asylums of the larger cities of the United States. He shows that the best records for conduct in the schools exist during clear, cool weather, and that crime is decreased under these conditions. Sickness and drunkenness occur more frequently during the colder months of the year.

The statistics are carefully compiled and extend over a number of years, being taken principally from institutions and bureaus of health and weather in the cities of New York and Denver. The results of these investigations are elaborately explained in the text, which is written clearly and lucidly, and are also graphically shown in a number of tables and charts. A. N.

THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Under the Editorial charge of GUSTAVUS P. HEAD, M.D. Vol. X., September, 1904. Chicago: The Year Book Publishers.

THIS volume of the series is devoted to typhoid fever and related infections, malaria, spotted fever, yellow fever, Malta fever, and diseases of the digestive system, with brief articles on typhoid pancreatitis, hysterical fever and adiposis dolorosa.

The article on typhoid fever contains an excellent compilation of statistics bearing on the value of the various symptoms, including particularly the urinary and serum reactions and the changes in blood pressure. The relation of the latter to the occurrence of perforation, a subject that is still in its infancy, is briefly reviewed in an interesting and instructive page. The authors also find a good deal to say about the treatment of typhoid fever, and altogether the chapter is an excellent condensation of the year's work, which has been quite productive in this disease. The greater part of the volume is devoted to diseases of the stomach and intestines. Fully twenty pages—a large number in proportion to the size of the book—are devoted to examination of the feces, a subject which “is too much neglected by American physicians, partly from the idea that the process is disagreeable on account of the disgusting odor and partly because the clinical value of such examinations has not been appreciated.” Apparently to emphasize their views the authors give a very complete essay on this important subject, taken chiefly from an article by Levi-Sirugue, which contains much that is not generally known or at least practised and should prove most interesting to practitioners, especially in children's diseases. As an epitome of the most recent work, the book shows the present trend toward rational methods of treatment by utilizing natural agents, such as food, water, heat and cold, mechanical stimulations and the like, being the external influences to which the body reacts in health and which therefore may be supposed to have as well some effect on the perverted vital processes in disease. A. N.

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INTERNATIONAL CLINICS. Edited by A. O. J. KELLY, A.M., M.D. Volume III., Fourteenth Series, pp. 302. Philadelphia: J. B. Lippincott Company, 1904.

ONE of the most interesting collections of papers upon syphilis which we have ever read is that to be found in this volume. The subject is presented from various standpoints, particularly those which appeal to the physician. The questions as to inoculation, differential diagnosis, fever, lumbar puncture and headache, the

nervous system in general, the laryngeal manifestations and tabes, hyperacute secondary nephritis which can be fatal, the fetal variety, the relation of suicide, together with the three therapeutic papers are satisfactory. The treatment of chancre, the hypodermic treatment of constitutional syphilis and the treatment of syphilis by calomel injections are excellent presentations of this part of the subject. The differences between the conclusions of Gottheil and Fournier in the last two are due to differences in methods and not in aims. In the section devoted to Treatment, Brown takes up the digestive disturbances occurring in pulmonary tuberculosis and gives such explicit directions that the patient can almost follow his advice. Boas on the rest cure in the treatment of chronic constipation offers a bit of special pleading to which some may take exception. The treatment of diabetes mellitus by Hood shows that the patient as well as his disordered metabolism must be considered. In medicine, Allchin offering rather diffuse observations on indigestion; Katzenbach, on mitral obstruction and chronic bronchitis, a well thought-out paper; Bishop on diseases of the liver based on extensive material; Duncan on scurvy, a vigorous refreshing of a time-worn subject, are all worthy of study. Surgery covers umbilical hernia of interesting type in difficult subjects, foreign bodies in the bronchi, the last word on lumbar puncture and a practical reposition of acute osteomyelitis and other sarcoma.

Gynecology is, as in earlier volumes, rather for the general practitioner and takes up the non-operative treatment of diseases of menstruation, hemorrhage at and after the menopause and some remedial agents used in this department of the healing art. The final paper and the only one in neurology is by Langdon on paralysis agitans, concise and definite.

The praiseworthy profusion of illustrations, which really illustrate, and the remarkable collection of papers on syphilis make the volume noteworthy, not only for present study but as well for future reference.

R. W. W.

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A TEXT-BOOK OF DISEASES OF WOMEN. By CHARLES B. PENROSE, M.D., Ph.D. Philadelphia: W. B. Saunders & Co.

THE fact that this book has reached the fifth edition since it was first published in 1897 is an eloquent testimony to its worth. For students, for whom it was intended, it is without doubt the best book we have ever seen. Its chief value rests upon its conciseness and clearness of description, thus enabling the salient points of diagnosis and treatment to be grasped without difficulty. From a rather intimate knowledge of the volume, gained while conducting

a quiz upon gynecology, we are in a position to very earnestly vouch for the utility of the book. The present edition has been carefully revised and there are several new illustrations as well as the addition of quite a little new matter, made necessary by the advance in gynecology since the earlier editions were published. As the intention of the author was to prepare a book especially for the use of the students, much anatomical and pathological detail, which he rightly considered to be better learned elsewhere, has been omitted and the question of treatment has been greatly simplified by making this portion of the subject express the writer's ideas alone.

W. R. N.

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PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Prof. of Therapeutics and Materia Medica in the Jefferson Medical College, Philadelphia, assisted by H. R. M. LANDIS, M.D., Assistant Physician to the Out-patient Medical Department of the Jefferson Medical College Hospital. June 1, 1904 and September 1, 1904. Philadelphia and New York: Lea Brothers & Company.

It is needless to say anything in a general way of *Progressive Medicine*, its merits being well known to the profession. The only change noticed is the paper binding of this year's issue. This change is not objectionable in a quarterly, especially as it is accompanied by a reduction of price.

The June edition contains a critical résumé of the literature on Surgery of the Abdomen, including Hernia, by Coley; Gynecology, by Clark; Diseases of the Blood, Diathetic and Metabolic Diseases, Diseases of the Spleen, Thyroid Gland and Lymphatic System, by Stengel; Ophthalmology, by Edward Jackson. This is a volume which appeals alike to the general surgeon, the special surgeon, and to the internist. The illustrations are especially numerous and good in the surgical portion of the book.

The September volume includes a critical résumé of the literature on the Diseases of the Thorax and its Viscera, by Ewart; Dermatology and Syphilis, by Gottheil; Diseases of the Nervous System, by Spiller; and Obstetrics, by Richard C. Norris.

Since medical literature has become so voluminous it is to be expected, especially if a man desires to be informed and up-to-date in the general literature of medicine, that there should be a demand for such a work as *Progressive Medicine*, and the publishers and authors of this series are to be congratulated upon the satisfactory manner in which this demand has been met. J. H. G.

SOCIAL DISEASES AND MARRIAGE. SOCIAL PROPHYLAXIS. By PRINCE A. MORROW, A.M., M.D. New York and Philadelphia: Lea Brothers & Co., 1904.

THIS book discusses diseases the very names of which to the lay mind savor so closely of indecency that they are ignored not only by school and college teachers of hygiene, but also by all State and municipal sanitary organizations. Yet these diseases are responsible for more acute crippling, chronic invalidism, suffering, and death than probably all the other contagious diseases combined.

The reason for terming this disease "social" is somewhat far to seek, but the term is one so commonly used that it is generally understood.

Morrow states that this book has for its fundamental purpose the study of the principles which should form the basis of the physician's conduct when he is compelled to consider in its concrete form the relation of venereal disease to marriage. In dealing with the various situations which present themselves in practice, certain rules are formulated for the physician's guidance.

Morrow condemns the dangerous optimism which has been responsible for untold misery. He believes the physician's first duty as a sanitarian is to protect others from infection and that this is higher than his duty as a physician to guard a guilty secret. The transmissibility of gonorrhœa in the married relation, and the effect upon both wife and offspring, are both pointed out, especial attention being directed to the inhibitory influence of this infection upon procreative capacity.

The relation of syphilis to marriage is given the careful consideration, which this subject deserves. Morrow believes the physician should use every effort to prevent the premature marriage of syphilitic men. If syphilis is acquired after marriage, and not from the husband, it is held the duty of the physician to guard the wife's secret, but only on condition that proper means will be taken to prevent contagion and that pregnancy is interdicted.

Morrow states that there is apparently no clear way in which the evil can be eliminated or materially lessened by the strong hand of repression. Moral crusades directed solely against women are abortive. The standard of social morals should be elevated, and the male libertine should be as rigidly suppressed as is the female, since there is nothing more untrue than the old adage that a reformed profligate makes a good husband.

As to educational measures, it is clearly recognized by physicians that a large proportion of venereal infections among the young grow as incident to ignorance of the risks of sexual commerce. Morrow feelingly alludes to the conspiracy of silence on the part of the public press, the clergy, and public educators in relation to these diseases. A policy of concealment follows the venereal patient to the grave.

The author holds that young men should be educated in a knowledge of sexual hygiene, and that this enlightenment should extend to the mass, and that this instruction should include as a cardinal feature a correction of the false impression instilled in the minds of young men that sexual indulgence is essential to health and that chastity is incompatible with full vigor. Attention should also be directed to the influence of alcohol in the instigation of immoral relations. It has been statistically shown that 76 per cent. of contaminations are effected under the influence of alcohol.

As to administrative measures, Morrow holds that the State can suppress the open and revolting manifestations of the vice, but that it cannot legislate morals into a nation. So far as the spread of venereal diseases is concerned, the State can render most effective aid by repressing charlatanism, which scatters broadcast its deceptive literature, and he suggests that it would be practical and feasible to demand a medical certificate from both parties contemplating matrimony as to the freedom of each from contagious sexual disease, with the imposition of a civil and penal responsibility for the transmission of venereal disease through marriage.

Morrow closes with a paragraph which sufficiently indicates the strength and motive of his book.

Upon humanitarian principles, in the interest of virtuous wives, who should no longer be poisoned with foul infections; in the interest of children, who should no longer be deprived of their rightful heritage of vitality and vigor; in the interest of the race, which should no longer be decimated and deteriorated, the dreadful curse of venereal disease should be lifted from the marriage relation.

E. M.

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DISEASES OF THE INTESTINES AND PERITONEUM. By PROF. DR. HERMANN NOTHNAGEL, Professor of Special Pathology and Therapy, University of Vienna. Edited, with additions, by HUMPHREY D. ROLLESTON, M.D., F.R.C.P., Physician to St. George's Hospital, London, formerly Examiner in Medicine in the University of Durham; Fellow to St. John's College, Cambridge, England. Authorized translation from the German under the editorial supervision of ALFRED STENGEL, M.D., Professor of Clinical Medicine in the University of Pennsylvania. Philadelphia, New York, London: W. B. Saunders & Co., 1904.

THIS volume on diseases of the intestines and peritoneum is most exhaustive in its study of their pathological conditions from all points of view—in other words it fulfils its definition as an encyclopedic work, taking up Pathology, Chemistry, Histology, Diagnosis, Symptoms, Course and Treatment.

Many diseases, both of the intestine and peritoneum, are dependent on or secondary to diseases elsewhere, and this fact alone widens greatly the scope of the work.

The author devotes two hundred and fifty pages to peritonitis, and of these one hundred are given to the much-written-about subject of appendicitis. His conclusions in this connection are in accord with the most advanced knowledge on the subject and are neither extreme nor reactionary. The great etiological factors, fecal concretions and bacteria, are placed on a plane of significance far above that of other causes, and the anatomical theories in regard to the occurrence of gangrene with such degree of frequency in this organ are most interesting.

On the subject of treatment, Professor Nothnagel expresses himself as opposed to early operation unless the assumption is well founded that the disease is of the rapid gangrenous or phlegmonous type. Those in favor of operation in all cases as soon as diagnosed support their view by quoting the histories of certain rapid fulminating cases in which the symptoms gave no indication of the gravity of the disease and where postponement of operation has proven a mistaken course. In view, however, of the rarity of these cases, and the possibility, in many instances, of the recognition of their true severity, it seems fair to balance the diverse opinions by placing in the opposite scale those cases where the operation itself has proved unnecessary and harmful.

Chapters on chemical processes in the intestine and on the bacteria of the intestine have been furnished by Drs. Fritz Obermayer and Julius Mannaburg, respectively, although the former does not receive credit in the index.

The editor acknowledges D'Arcy Powers' assistance in making additions to the section on Intussusception.

This volume should prove a most valuable reference book to the profession at large as well as to the internist. J. N. H.

HOW TO COOK FOR THE SICK AND CONVALESCENT, ARRANGED FOR THE PHYSICIAN, TRAINED NURSE, AND HOME USE. By HELENA V. SACHSE, M.D. Philadelphia: J. B. Lippincott Co., 1904.

THE present new edition makes this one of the most useful books on the subject of dietetics so far published. The classification of recipes for reference is in a complete form, making it easy for both the trained and untrained person to arrange the different diets ordered by the physician. The recipes are in appropriate proportions when needed in preparing dishes for one patient. As a text-book for nurses in private practice it is invaluable. M. E. S.



THE PRACTICAL APPLICATION OF THE ROENTGEN RAYS IN THERAPEUTICS AND DIAGNOSIS. By WILLIAM ALLEN PUSEY, A.M., M.D., and EUGENE W. CALDWELL, B.S. Second edition. Philadelphia: W. B. Saunders & Co., 1904.

THE practical value of this work is demonstrated by the appearance of a second edition so soon after the first. The author's method of literature review and bringing his subject up to date is of particular value. There are, however, certain definite advances in the knowledge of the therapeutic application of the Roentgen rays that have not been included. We refer particularly to the adaptation of the qualities of Roentgen energy to the various forms of malignant disease, adapting the quality to the character and situation of the diseased tissue. A more accurate measurement of dose is also now possible, as has been demonstrated in recent foreign publications.

The estimation of the quality of the ray by the fluoroscopic image of the hand upon the screen, as advised, cannot be too severely condemned. To this practice can be attributed the grievous necessity recently reported of amputating the hands of two successful operators in this field of work. The danger to the operator and patient should receive more careful treatment in a work intended for instruction in this subject.

C. L. L.

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THE HUMAN STERNUM. Three Lectures Delivered at the Royal College of Surgeons, England, November, 1903. By ANDREW MELVILLE PATERSON, M.D., Derby Professor of Anatomy in the University of Liverpool, Hunterian Professor at the Royal College of Surgeons of England. London: Published for the University Press of Liverpool by Williams & Norgate, 1904.

THIS monograph deals in a most thorough manner with the sternum from the point of view of the anatomist, morphologist, and embryologist. Notwithstanding the fact that the author makes no claim to present a "complete account" of the subject, he nevertheless offers the reader an amount of information on this subject which will surprise most of us. The work is the outcome of many years of study and is deserving of the strongest commendation.

One of the points brought out by the author is that the sternum should be regarded as evolved, developed and constructed rather in relation to the shoulder girdle than to the thorax. He also believes that there is no solid evidence of the ontogenetic or phylogenetic origin of the sternum from the ribs and that its connection with these structures is secondary. The book is well illustrated and the text is most comprehensive.

J. H. G.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**The Question of Cytodiagnosis.**—NIEDER and MAMLOCK (*Ztschr. f. kl. Med.*, 1904, H. 1 and 2). French writers, notably Widal, Sicard, and Ranout, have recently laid much emphasis on the histological examination of the spinal fluid as an aid in the diagnosis of certain diseases of the brain and cord. The essential change consists in an increase in the number of small mononuclear cells and there is now a large number of contributions from French and German sources bearing upon this relation in the most varied affections of the nervous system. After thorough centrifugalization the sediment, if any be present, or in its absence, the last few drops of fluid in the tube, are spread upon a slide, stained and examined. Nieder and Mamlock recommend simple methylene blue staining as the most satisfactory. In the examination of a large number of fields with a 400 to 450 power, an average of over 3 to 4 lymphocytes to the field is considered abnormal by the French authors. Merzbacher gives 6 to 8 as the upper normal limit. From the reports previously published an increase in the lymphocytes has been found in progressive paralysis, tabes, cerebrospinal syphilis, certain cases with choked disks, syphilitic headache, syphilitic hemiplegia, herpes zoster, sciatica, and parotitis, and an absence of increase in poliomyelitis, syringomyelia, hemiplegia of old age, polyneuritis, functional neuroses, compression myelitis, cerebral tumors, and epilepsy. Cases of general paralysis, of tabes, and those with syphilitic lesions present the most constant and most marked increase, but even in these the increase is apparently intermittent and paroxysmal. Siemerling has reported a case of general paralysis in which three successive punctures failed to show a lymphocytosis, and Nieder and Mamlock cases in which, while absent on one examination, it would appear on a later.

In 9 cases of tabes examined by Nieder and Mamlock there was an

increase of lymphocytes in 5; of 6 cases of hemiplegia, an increase in 4; all four positive cases gave a definite syphilitic history, the two negative ones being non-syphilitic hemorrhages of old age. Evidently the syphilis and not the apoplectic insult causes the lymphocytosis, and this is in accord with previous reports of French writers. Even in a case of severe secondary syphilis without nervous manifestations a striking increase in the number of lymphocytes was found. Punctures in a case of fibrinopurulent arachnitis were constantly negative; in case of uræmia with convulsions there was a moderate increase; two cases of tetanus were positive, one being associated with a large number of polymorphonuclear leukocytes. Results were negative in a case of spinal trauma and in cases of alcoholic neuritis, traumatic neuroses, double sciatica, and transverse myelitis.

Although meningeal irritation has been assumed as the cause of the lymphocytosis, Nieder and Mamlock urge that it is not the only factor of importance. They believe that intoxication plays an important rôle, namely, "when there is a continued irritation of the central nervous system by a constantly developed or continuously renewed virus." This would explain the positive results in syphilis, tetanus, and uræmia and the negative results in epilepsy, hemiplegia, and coma. They also believe that a constant mechanical irritation may cause a lymphocytosis. There was a very striking increase in one case of brain tumor and in another of a cervical cord tumor, neither of which were syphilitic.

In two rabbits small air balloons were introduced beneath the skull to simulate the pressure of tumors and in both there was produced a moderate but definite lymphocytosis.

From the results already published the evidence is seen to be not only variable but in some instances even contradictory. As a diagnostic method it has not fulfilled what was originally anticipated. Perhaps the methods will be perfected, and as experience enlarges its limitations better defined. Its most promising field would seem to be in syphilis, as it has been shown that a lymphocytosis occurs in this disease even in the absence of nervous lesions. How early and under what conditions it occurs need still to be studied.

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**The Relation of Diabetes to Albuminuria and Renal Disease.**—Dr. BERNARD VAS (*Wiener klin. Wochenschr.*, 1904, No. 30, p. 841). The percentage of cases of diabetes in which albumin occurs in the urine is variously stated, and the significance of the albumin disputed. Schmitz gives 67.7 per cent.; Lecorché 50 per cent., Bouchardat 45 per cent., Grube 40 per cent., Pollacsek 36.7 per cent., Naunyn 34 per cent., Noorden 23.5 per cent. The statistics published by Aldehoff are especially valuable as they comprise microscopic examinations which the others do not. In 680 cases of diabetes albumin was constantly present in 540 or 79.4 per cent, and transiently present in 140 more, or 20.6 per cent., leaving only 9 cases uniformly free from albumin (evidently some inaccuracy here). Casts were found in 70 per cent. of the cases. Out of 1821 different specimens of diabetic urine Vas found albumin in 77.27 per cent., but casts in only 19.05 per cent. The amount of albumin present was seldom a measurable quantity, usually only a trace and its occurrence bore no relation to the amount of sugar. The striking variation in the statistics above given Vas thinks can be largely explained by the different methods of examina-

tion used and the difference in the interpretations of the results. Albuminuria in diabetes may be divided into two classes: those in which it depends essentially upon the disease itself and those in which it is a symptom of some concomitant organic lesion. In the second class are grouped cases associated with cystitis, pyelitis, and pyelonephritis and febrile albuminurias. Also the albuminuria of gout and arteriosclerosis following excesses in alcohol or dependent on cardiac insufficiency. Naunyn includes agonal albuminuria. The frequent association of diabetes and gout as pointed out by Garrod and Charcot has been abundantly confirmed. In Grube's 177 cases 16 had gout and 23 more gave a family history of gout. Often the gout precedes the diabetes and the arthritic attacks stop completely when the diabetes becomes established. More frequently, however, the two diseases occur together. In these cases as well as in those with advanced arteriosclerosis the diabetes is not held accountable for the albuminuria. In other cases, however, the albuminuria seems to bear a close relation to the glycosuria and these Vas divides into three groups: (1) Albuminuria without any evidence clinically or morphologically of renal changes; (2) albuminuria usually with more abundant albumin and with casts evidencing some structural lesion in the kidneys but clinically without renal symptoms; (3) albuminuria with clinical as well as morphological evidence of nephritis. Cases belonging to group one are the most numerous and Grube classes the condition as a functional albuminuria. The amount of albumin is usually very small and frequently its presence is intermittent, disappearing or becoming much reduced; when following a careful diet the amount of sugar falls. Stokvis blames the rigid dieting as the cause of the albumin but Külz and Naunyn deny this. Schütz accepts two causes, the increased egg consumption and the vesical catarrh caused by the fermentation of the glucose in the urinc. Grube and Senator approve the first, but Naunyn was unable to confirm it. The second is supported neither by clinical nor pathological evidence. Although the condition is spoken of as functional albuminuria definite renal lesions have been described in many cases as large, hyperæmic kidneys, increase of connective tissue about the glomeruli, degeneration of the epithelium in Henle's loops, epithelial necrosis, etc. Cases in the second group have usually shown for a long time marked glycosuria. The amount of albumin varies between wide limits but can generally be estimated quantitatively. The sediment contains hyaline and granular casts—often in abundance. Clinically there are neither cardiac nor renal symptoms. The amount of albumin and of sugar in the urinc frequently vary directly with one another, the albumin falling as the sugar rises and vice versa, and this relation may exist for years without any evidence of the abatement of the glycosuria as often happens when a true nephritis develops. The significance of these cases is little understood and careful pathological records are scanty. In cases belonging to the third group there is evidence, clinically and anatomically, that the albumin depends upon structural changes in the kidneys. Senator ranks diabetes as a cause of interstitial nephritis. Grube thinks the polyuria may act as a form of continuous irritation leading finally to epithelial and interstitial changes. Nephritis is always a serious complication in diabetes, and as the symptoms become more prominent the glycosuria frequently recedes until the picture is dominated by the renal manifestations. Clinically, in such

cases hypertrophy of the heart develops, œdema sets in, the specific gravity of the urine rapidly falls to 1010, or even 1005, albumin and casts are more or less abundant, and the series of events usually culminates in uræmia. These cases are evidently of great interest in relation to the whole question of the pathology of diabetes. Does the nephritis influence the disease itself or does the disease remain and the kidneys through some structural change refuse to pass the sugar? That the kidney lesion does in some way interfere with the excretion of sugar has been suggested by experiments on animals and man, but the results are not constant and the evidence is insufficient to give an authoritative answer.

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## SURGERY.

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UNDER THE CHARGE OF

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**Trephining under Local Anæsthesia with Separation of the Membrane without Hemorrhage.**—HEIDENHAIN (*Centralblatt für Chir.*, 1904, No. 9) states that the use of either a  $\frac{1}{2}$  or a 1 per cent. solution of cocaine with about  $\frac{1}{2}$  a drop of 0.1 per cent. solution of adrenalin will secure good anæsthesia of all tissues which has a duration of hours. This solution is infinitely better than Schleich's fluid, the effect of which soon disappears. Braun's solution will produce anæsthesia of the bone and cerebral membranes. The author notes in detail two cases in which he used the method with success—one of syphilitic necrosis of the skull and the other, one of recurrent sarcoma in the motor region of the brain. In each case the anæsthesia was perfect. From the excellent results in these cases the author states that he believes that even more major operations may be undertaken successfully under local anæsthesia. The maximum dose of cocaine in use in Germany is 0.05. In operations upon the trunk and extremities, Heidenhain has never exceeded this dose, as larger quantities are distinctly dangerous. Care must be taken that the patient is in a horizontal position during the operation and this position should be maintained for at least an hour after the operation. It is also advisable that some food be taken previous to the operation and during it a cup of coffee, containing a small quantity of an alcoholic stimulant should be taken and after the operation a cup of thick soup should be eaten. Bleeding from the membranes may be considerable after the operation. The incision in the membranes should be closed, care being taken to include any bleeding points by suture ligatures. In all cases union occurred by the first intention.

**Cholecystenterostomy with the Formation of an Artificial Gall-duct.**—**KRUKENBERG** (*Centralblatt für Chir.*, 1904, No. 5) states that he was obliged to operate upon a man, aged seventy-eight years, who had for years suffered with severe abdominal pain. Examination showed a lump in the region of the gall-bladder. There was no history of the passage of gallstones. Jaundice was marked and permanent. The liver was markedly enlarged and the gall-bladder was palpable as a tumor, exquisitely tender, and about the size of a hen's egg. The usual incision was made and the gall-bladder exposed and opened. It was found to contain much thick bile and some small gallstones. After thoroughly flushing out the gall-bladder the jejunum was brought over, opened by an incision 1 cm. long, and the fundus of the gall-bladder inserted and maintained in place by Lembert sutures. The wound was closed in the usual manner without drainage. The operation was a complete success, the patient making an uninterrupted recovery.

**An Operative Method of Reduction of Old Irreducible Dislocations of the Hip-joint.**—**RYDYGIER** (*Centralblatt für Chir.*, 1904, No. 13) states that while there can be no doubt that reduction by operation is really the ideal method of treatment in these cases, the greatest danger is that of infection which may also follow the bloodless method. Care should be taken, no matter what method be used, that the parts are bruised just as little as possible, for this of necessity lowers the vitality of the tissues and their ability to withstand infection is proportionately decreased. The author strongly recommends the method by means of a large flap which extends 6 to 7 cm. below the trochanter and which is extended backward as far as the posterior superior iliac spine, parallel to the fibres of the gluteus maximus. The anterior portion of the flap is extended upward between the tensor of the fascia lata and the gluteus medius up to the anterior superior iliac spine. This fully exposes the field of operation and permits an accurate dissection to be made with the least possible amount of damage to the tissues surrounding the joint.

**Lessening the Deleterious Effects of Pneumothorax in Intrathoracic Operations.**—**SAUERBRUCH** (*Centralblatt für Chir.*, 1904, No. 6), after mentioning the admirable work in this line that has been done by Mikulicz, states that he has experimented on rabbits and dogs in order to ascertain the blood conditions, the type and force of breathing, with and without artificial respiration, and as a result noted eight conditions which may seriously complicate the situation: (1) Change in the breathing, causing a variation in the size of the lung. (2) Interstitial emphysema which may result from artificial respiration. (3) An enormous loss of heat, especially where artificial respiration is resorted to; this may be as great as 3° in half an hour. (4) A marked reflex effect upon the circulation. (5) The pneumothorax may either continue or return after the cessation of artificial respiration. (6) It may be necessary to do tracheotomy which distinctly increases the chance of pneumonia developing. (7) Narcosis may complicate. (8) There is great danger of infection of the pleura as the result of the constant circulation of air in the pleural cavity. In an effort to avoid the dangers of pneumothorax, the author experimented on animals in a specially constructed

room in which the operator and his assistants and the body of the animal were in this room while the animal's head was outside. Proper provision was made for ventilation, which prevented the temperature from becoming unbearable. It was found possible to do the most severe operations on animals, which included opening the mediastinum and pericardium without pneumothorax developing. The author states in conclusion that he is now at work on the physiological aspects of this method and that he hopes to submit his results in the near future.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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**The Treatment of Œdema of the Legs in Heart and Renal Diseases.**  
 —DR. CAPITAN recommends in this connection the use of the thermocautery. The sharpest and most slender of tips heated to a dull red is used. With this a quick puncture down to the aponeurosis is made on either side of the calf. Rarely does this cause hemorrhage, and serum soon begins to exude from the punctures. The patient receives immediate relief, which is augmented as time goes on. The swelling lessens and the heart action is ameliorated. If the perforations close, it is necessary to open them again. If they are kept open the serum flows without ceasing. The patient is confined to his chair, and his legs should be thickly and tightly bandaged. At least three times a day the bandages should be removed, and the legs having been washed in boric acid solution and smeared with vaselin, dry dressings should be applied. It is necessary to exercise great attention in the care of the legs, for erythemata and even erysipelas have been known to result. Some patients prefer to go without the bandages and have the limbs covered only with something spread over the knees. The author has seen one cure follow this treatment, but in most cases only relief is effected, and he is doubtful whether such patients are truly benefited, since by the procedure, while the patients are relieved for the time being, their agony is only prolonged and the end deferred. He believes, however, that when œdematous legs are punctured, it should be done with the thermocautery.—*La médecine moderne*, 1904, No. 36, p. 283.

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**The Treatment of Albuminuria.**—MM HUCHARD and FIESSINGER consider that in albuminuria of hepatic origin alkalies and laxatives are indicated; in that of intestinal origin laxatives, farinaceous foods and a diminution of the milk ingested; in that of essentially gastric origin a

diet of milk and vegetables and warm baths. In albuminuria due to syphilis, it is wise to give specific treatment in small doses, especially at first. In albuminuria of toxic origin the indication, above all, is to suppress the poison. The poison, however, is frequently of endogenous origin. In diabetes, for example, we may distinguish two forms, functional and organic. In the former we treat only the diabetes. In the latter both factors are to be treated. Here the diet of meat may be dangerous, and we must prescribe milk, vegetables, eggs, and a reduction of the chlorides. Excellent results may follow the administration of sodium arsenate, in dosage of  $\frac{1}{6}$  a grain per day, in connection with sodium bicarbonate. Gouty albuminuria also is of two varieties; in this we cut off milk, which is likely to increase intestinal fermentation. Meat diet, especially red meat, is to be avoided. Alcohol is harmful, but green vegetables are allowable. In the cyclic albuminuria of children, which may result in incurable lesions in the adult, overfeeding is to be avoided. Cardiac albuminuria, early or late, is found, both in the child and the adult. In the early form theobromine is indicated; in the tardy, digitalin. In the latter case, if the heart muscle is the seat of degeneration, the dose should be small. In the albuminuria of neurasthenies due to hepatic or digestive derangement, warm showers, lasting three to five minutes, are to be employed. In patients beyond middle life, albuminuria, with galop rhythm and tense pulse, is to be treated by a diet of milk and vegetables, theobromine, and small doses of digitalin prolonged for months at a time. Bouillon made from the kidneys of swine has given various results in the hands of various observers, probably due to the fact that an active preparation of this sort is difficult to obtain.—*Journal des praticiens*, 1904, Nos. 35 and 36, pp. 594 and 562.

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**Phosphoric Acid.**—DR. F. CAUTREE asserts that this acid produces especially good results in patients with urinary hypoacidity. In neurasthenic states, as well as in the various disturbances attendant upon pregnancy, and in chlorosis it is indicated. In arthritis patients good results are effected, providing the urine is watched for hyperacidity. In diabetes this manifestation should be guarded against also. In chronic rheumatism, as well as in arthritis deformans, the drug yields good results, as well as in eczema, psoriasis, acne, etc. In cachectic states, in convalescence, and in the anæmias of hot countries the acid acts well. In hyperchlorhydria it acts locally by restraining the secretion of hydrochloric acid and in hypochlorhydria it replaces the diminished or absent normal acid. It retards abnormal acid fermentations, aids digestion, and increases the pancreatic and duodenal secretions. The acid is never toxic, as is the metal from which it is derived, a conclusion at which the author has arrived after extensive use of it in therapeutics and animal experimentation. The dosage should never exceed 30 to 60 drops daily of a 36 per cent. solution of the anhydrous acid. Beginning dosage should be small.—*La Presse médicale*, 1904, No. 74, p. 588.

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**Anhydro-oxymethylene-diphosphoric Acid in Therapeutics.**—MM. A. GILBERT and A. LIPPMANN consider the salts of this acid are indicated, and have most excellent effect in all conditions in which there are pathological manifestations due to defective assimilation of phosphorus



from the digestive tract and all states in which general nutrition is defective. They prescribe the magnesium and calcium salts of the acid in dosage of about 30 grains daily for the adult. The agent possesses not only purely nutritive qualities, but also dynamic properties, which produce an excitation of the nutrition of the tissues of the cell of the organism. The authors report cases of chlorosis, pulmonary tuberculosis, prolonged convalescence from acute diseases, osteomyelitis, neurasthenia, etc., in which the exhibition of the salts of anhydro-oxymethylene-diphosphoric acid have given most excellent results.—*La Presse médicale*, 1904, No. 73, p. 577.

**The Treatment of Diabetes Insipidus.**—DR. B. STEIN, after trying various drugs recommended for this malady—valerian, antipyrin, arsenic, opium, atropine, etc.—with very little effect, has treated a very resistant case with subcutaneous injections of strychnine. After twelve injections the quantity of urine was diminished from 15 to 12 quarts daily, during the four following weeks it was progressively diminished to  $3\frac{1}{2}$  to 4 quarts; its specific gravity was about 1005. The polydipsia became less marked, and the body weight increased, and the patient, who had been able to walk only for a short time, became able to walk for from three to five hours. Healthy slumber also returned. The author commenced the treatment by injecting 0.015 grain of strychnine nitrate daily for five days, then after a remission of three days, 0.045 grain were administered for a week; then another three-day remission followed by a week of injections of 0.075 grain doses. During the fourth week 0.15 grain was injected. There were no ill-effects from the treatment other than pain at the site of the needle punctures. It is important to commence with small doses and to gradually increase them. The strychnine seems to act directly upon the disease, not alone upon the polyuria, but the reason for its action is difficult of explanation.—*Münchener medicinische Wochenschrift*, 1904, No. 36, p. 1606.

**Disinfection of the Gall-ducts and Internal Antisepsis.**—DR. F. KUHN has arrived at the following conclusions, after experiments upon the fermentation of the bile in the gall-ducts. All liquid bile which is produced through fistulæ ferments to a greater or less extent when allowed to stand in the test-tube for from twenty-four to sixty hours. Bile which is secreted during the internal administration of sodium salicylate, menthol, or thymol, ferments more slowly and to a less degree depending upon the character and dose of the drug administered. This anti-fermentative action needs a day or two for its establishment, depending upon the rapidity with which the drug is absorbed, and persists as long as the drug is administered. Experiments showed salicylic acid and its salts to be the most active agents in delaying biliary fermentation, and consequently to be the agents of choice in inflammations of the biliary passages.—*Münchener medicinische Wochenschrift*, 1904, No. 33, p. 1457.

**Diet in Hepatic Lithiasis.**—DR. W. CLEMM, having in mind the theory that bacteria will not thrive in a gall-bladder unless there is stasis of bile, advises prophylaxis and treatment through re-establishing normal secretion of bile by means of hygiene and proper diet. A proper diet is one rich in fat. Saponifying substances markedly influence

the composition of the bile and cause cholesterinc calculi to soften and diminish in size. Consequently, the author advocates a diet of milk, cream, butter, yolk of eggs, and fat meats. In feeble patients cod-liver oil is advisable. Mayonnaise is to be avoided, but vegetables cooked in fat and all forms of cake and biscuits are allowed. The fat used in cooking should be animal not vegetable. Exclusive milk diet is to be avoided, for it is likely to favor constipation. The need of carbohydrate food is supplied by green vegetables, potatoes, fruit, and bread crust. As alcohol does not influence the secretion of bile, its temperate use is allowable. The drinking water should be carefully chosen, since cases in which there existed calculi composed of silicates from this source have been recorded. As an adjunct to the saponifying diet, sodium oleate, and inunctions of soapy substances are useful.—*Die Heilkunde*, 1904, No. 6, p. 241.

**Isopral, a New Hypnotic.**—DR. ESCHLE has used this remedy in 50 patients affected with mental diseases and has proven its hypnotic value, especially in cases where chloral and morphine are contraindicated. Its dose is about  $7\frac{1}{2}$  grains, either in powder or alcoholic solution. In painful affections, dyspnoea, cough, etc., its action resembles that of chloral, but is more rapid. Untoward symptoms due to its use, especially upon the nervous system, the digestion, and the heart, were not noticed.—*Fortschritte des Medizin*, 1904, No. 6, p. 237.

**Stovaine as a Local Anæsthetic.**—M. RECLUS, after employing this agent in 100 cases, concludes that the drug possesses at least as strong analgesic power as does cocaine, and is more powerful in this regard than any other substance which has been used in place of the latter drug. None of the toxic symptoms which have been observed as due to cocaine occur with stovaine. In one case the author observed slight pallor and præcordial anxiety. A dose of three grains may be used, showing that the drug is less toxic than cocaine. Stovaine is, unlike cocaine, a vasodilator.—*Le Progrès médicale*, 1904, No. 28, p. 27.

**The Treatment of Prostatitis.**—DR. POROSZ advocates the use of faradism in this affection. A small electrode is placed in the anus and a larger one upon the abdomen. At first the current should be very weak, but may be strengthened as the patient becomes accustomed to it. The current causes the muscular tissue of the gland to contract and so expel the retained secretions. The author considers this treatment applicable to all acute cases.—*Wiener medicinische Presse*, 1904, No. 13, p. 627.

**Guaiacol as a Dressing for Suppurating Wounds.**—DR. P. N. PROKHOROV has employed, in the dressing of suppurating surfaces, gauze, upon which 20 or 30 drops of pure guaiacol have been sprinkled. With such dressings he has treated different forms of suppuration, among others, large phlegmons of the extremities with gangrenous spots, gaseous infiltration, and deep necrosis, with excellent results.

DR. V. BIALOBJESKY, in a case of disarticulation of the shoulder for gangrene of the arm, was able to arrest the gangrene, which had already involved the pectoral muscles by means of compresses of gauze saturated with guaiacol.—*La semaine médicale*, 1904, No. 40, p. 320.

## PEDIATRICS.

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UNDER THE CHARGE OF

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AND

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**The Channels of Infection in Tuberculosis in Childhood.**—L. KINGSFORD (*Lancet*, September 24, 1904) has analyzed the post-mortem records of 339 cases of tuberculosis of all ages up to fourteen years, taken from the East London Hospital for Children. The records show that 48 per cent. occurred during the first two years, and 80 per cent. during the first five years of life. The writer reviews the recognized modes of infection: 1, inhalation; 2, ingestion; 3, inoculation, and 4, placental; the last two being exceedingly rare, are not given practical consideration.

Although experimental evidence tends to show that the inspired air is free from foreign particles by the time it reaches the larynx, still, when particles are present in great numbers, it is possible for them to be inhaled even into the alveoli. This possibility is well shown by the fact that 49 per cent. of the cases were infected apparently through the mucous membrane of the trachea or larger bronchi. Ingested bacilli are liable to settle on any part of the alimentary tract, so that the mouth, fauces, and pharynx are thus common to both inhalation and ingestion. Bacilli passing through mucous membrane at any point are soon found to be present in the adjacent lymphatic glands. The frequency of lymphatic gland infection in children is shown by the fact that in 90 per cent. of the writer's cases the lymphatic glands were involved, while in 68 per cent. they were the primary foci. That the lymphatic glands may be secondarily infected through the blood stream is also considered. The probability of the bronchial glands being primarily infected by bacilli entering originally through the intestinal wall is thought unlikely, for of 64 cases where the origin was obviously in the abdomen, only 18 showed tubercle in any of the glands in the thorax, while the mesenteric glands were caseous in 62.

The cases have been divided by the writer into three main groups, namely, thoracic, abdominal, and pharyngeal, according to the location of the oldest or primary focus. The thoracic cases number 212, or 62.5 per cent. of the total number. In 34 of these cases the oldest lesion was in the lungs; in 167 in the thoracic glands, and in the remaining 11 the lesions in both seemed to have been of the same age. This group is subdivided into: 1, cases which showed no lesion in the intestine or mesenteric glands; 2, cases which showed old lesions of the thorax, but also early involvement of the intestines or mesenteric glands, and 3, cases which were certainly thoracic originally but which showed intestinal lesions further advanced than the preceding subdivision.

The second group comprises those which showed the primary lesions in the intestines or mesenteric glands. These cases number 64, or 18.8 per cent. of the total. These are further divided into: 1, cases which showed no thoracic lesions; 2, cases originating in the intestines, but showing evidence of recent thoracic infection, and 3, cases originating in the abdomen, but showing more advanced thoracic disease. Of the 64 abdominal cases, 26 seemed to begin in the intestines and 29 in the mesenteric glands, while in 9 the lesions apparently commenced simultaneously in both.

The writer calls attention to the abdominal cases in reference to the ages of the children. Only 10 per cent. of the cases in the first year were abdominal in origin, 17.5 per cent. in the second year, 31 per cent. in the third year, and 16 per cent. in the fourth year, or an average of 18.1 per cent. for those years, as against 18.8 per cent. for all ages. Thus, instead of the proportion of abdominal cases to the total cases of tubercle being greater in the first four years, with the exception of the third year, the figures are lower than the average at all ages. Still's figures correspond closely with the above.

The frequency of primary abdominal tuberculosis among children in Great Britain is noted, and the figures compared with the reports from other countries. Of 1119 cases of tuberculosis collected in Great Britain, 214, or 19.1 per cent., were primary abdominal cases; in the United States only 13 cases of 434 were abdominal in origin; while in France and Germany ten observers have recorded only 9 cases out of 364, or 2.5 per cent. A satisfactory explanation of the greater frequency of abdominal tuberculosis in Great Britain than on the continent is not forthcoming. The writer believes that the more general use of sterilized milk and better inspection and regulation of cattle may partly explain it. But when considering the possibility of cows' milk being responsible for this high percentage of abdominal cases, attention must be called to the class of children under consideration. The writer's cases were all drawn from the poorest families of the East End of London, by whom cows' milk is considered an expensive article of diet. When milk is used it is usually boiled or "scalded," but more often its substitutes—condensed milk and patent foods—take its place. Consequently, the chances of a child taking any quantity of virulent tubercle bacilli with the milk are greatly diminished. As two years is about the limit of milk age in this class, it follows that primary abdominal tuberculosis should be most pronounced in the first two and a half years of life (allowing an incubation period of some months), since most milk is taken during that period. It has, however, already been seen that primary abdominal tubercle is proportionately less frequent during these years than in the later years of childhood.

The next group (pharyngeal cases) includes 13 cases infected through the fauces, pharynx, naso-pharynx, or middle ear. Of these, the middle ear was responsible for 4, the pharynx or fauces for 5, 1 of these originating in the tonsil. The origin of the remaining 4 cases was not so clear, as the tracheal glands were caseous, but the pharynx was probably the seat of entrance. The number of cases infected through these channels is considerably underestimated, since only a small proportion of the cases ever reach the post-mortem room, as the disease usually remains localized and is frequently cured.

A large group of cases of doubtful origin, 50 in number, remains, and

includes cases where the peritoneum alone, the liver or spleen only, the spine or the hip-joint alone, showed tuberculous lesions. Also cases in which the lesions in the thorax and abdomen were too far advanced to give any clue as to the method of infection.

In conclusion, if the middle-ear cases are regarded as infected by inhalation, the tonsil case as an alimentary infection, and the remaining pharyngeal cases as doubtful, then inhalation would account for 216 cases, or 63.7 per cent., and ingestion for 65, or 19.1 per cent., the remaining 17 per cent. being of doubtful origin.

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## OBSTETRICS.

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UNDER THE CHARGE OF

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**The Treatment of Accidental Hemorrhage.**—At the last meeting of the British Medical Association, MACAN (*British Medical Journal*, 1904, No. 2286) read an interesting paper upon this subject which received full discussion.

This condition arises from accident, from disease, and from some failure in the mechanism of labor. As regards the mechanism of accidental hemorrhage, he finds that the healthy uterus cannot be distended to any considerable extent by blood pressure. The placenta has great power of accommodating itself to changes in size of its site, and is not so easily separated as the membranes. Gravity and peristaltic action of the uterus need not be considered. In spreading, the hemorrhage will follow the line of least resistance.

Accidental hemorrhage is caused by increased action of the heart, obstruction to the return of venous blood to the uterus, disease of the uterine vessels, sudden lessening of intrauterine tension and diminution in size of the placental site. When the heart action is slowed, the tendency of the hemorrhage is to stop; increased intrauterine tension from effused blood or intrauterine contraction or adhesions also tends to stop the bleeding. The formation of thrombi produces a like result.

On the other hand, increased heart action, fresh separation of the placenta, diminished coagulability of the blood, a very rapid flow of blood, with adhesions between the placenta and membranes to the uterine walls, tend to increase the bleeding. Diminished intrauterine tension has an important bearing and may arise from the giving way of the uterine walls, the absence of uterine contractions, blood escaping from beneath the placenta or rupture of the membranes.

Where hemorrhage is but slight and from the centre of the placenta it may remain internal. Adhesions between the placenta and membranes or wall of the uterus, distensibility of the uterine wall and the

presenting part acting as a plug tend to cause the hemorrhage to remain internal. When these conditions are not present, especially when the bleeding begins near the margin of the placenta, blood will escape externally.

It is very important in these cases to consider the effect of rupturing the membranes and the effect produced by contractions of the uterus on the hemorrhage.

Rupture of the membranes lessens intrauterine tension and tends to increase hemorrhage. Uterine contractions do not cause hemorrhage to stop, for it is not the contraction of the womb but its retraction which controls bleeding. Uterine contractions may cause hemorrhage when the contraction ring is high in the abdomen and the site of the placenta is lessened, when there is delay in the birth of the after-coming head or when a shoulder presentation is neglected. After the birth of the first of twins, or where excessive amniotic liquid escapes, the uterus often contracts but does not retract and hence hemorrhage arises. During a contraction, hemorrhage is arrested if the supply of blood is cut off and intrauterine tension is increased.

As regards diagnosis, we cannot distinguish between a low insertion of the placenta with bleeding and external accidental hemorrhage. In recognizing internal hemorrhage, when symptoms of shock with abdominal pain are present, we must suspect hemorrhage but frequently we cannot diagnose it until after the expulsion of the placenta. When the hemorrhage is concealed, we appreciate its nature from the fact that the symptoms are out of all proportion to the quantity of blood lost. It is of great importance to know if possible how much of the hemorrhage is internal.

In the matter of treatment, we may hope to prevent this accident by curing endometritis, by lessening arterial tension and venous congestion, by dealing with nephritis and by giving remedies which shall increase the coagulability of the blood.

In the treatment of hemorrhage itself, we try to arrest hemorrhage without emptying the uterus if possible. This may be attempted by placing the patient at absolute rest, giving opium and lessening congestion by salines. We may prevent the escape of blood by firmly tamponing the vagina or cervix and by making firm pressure on the uterus, either by the hand or with the vaginal tampon and abdominal binder, aided by a perineal compress and bandage we may increase uterine tension, thus causing the hemorrhage to cease; measures which retard the flow of blood help in the formation of thrombi.

Macan believes in the Rotunda method of tamponing for this condition. This method has been developed by Purefoy, a master of the Rotunda, as follows: For tamponing, sterilized cotton-wool in masses the size of a large walnut, soaked in an antiseptic solution, is used. After preliminary cleansing and the use of the catheter, the fingers of one hand are used as a speculum, the tampons are wrung dry and packed firmly about the cervix. This is done as tightly as possible until no more can be introduced into the vagina. A large strip of iodoform gauze is then placed over the tampons, projecting from the vagina and forming a firm perineal pad. A strong binder is firmly pinned from above downward, starting above the fundus, and to this is added a firm perineal bandage, the whole making very tight compression. The after treatment consisted of warmth, warm liquid food

and one-half grain of morphine hypodermically; the physician is notified if uterine contractions begin, if the perineal pad begins to bulge, if hemorrhage comes through the dressings or if the patient grows faint. Of 43 cases so treated, 2 died; one undelivered from hemorrhage, the other from rupture of the uterus. In conducting labor in these cases, the membranes must not be ruptured if possible. If pains become vigorous, the perineal bandage and part of the tampons should be removed. The contractions of the uterus will force out the remainder and the membranes should not be ruptured until full dilatation is secured.

In summing up his paper, Macan states that, from his personal experience, he is entirely in favor of performing Cæsarean section in these cases in preference to rapid dilatation of the cervix. He would be in favor of vaginal Cæsarean section.

He believes that rupture of the membranes is not good treatment of this complication unless it causes rapid expulsion of the child. Where during labor the membranes persist unbroken in the second stage and hemorrhage begins, such bleeding is immediately controlled by rupture of the membranes and the termination of labor.

Galabiu has seen accidental hemorrhage completely internal from partial degeneration of the placenta with living fetus. He believed that rupture of the membranes is followed by increased intrauterine tension and hence that it tends to diminish hemorrhage. He did not find on examining the statistics of the Rotunda before treatment by tamponing was introduced a very great improvement in the mortality. He thought Cæsarean section might in some cases increase shock to a fatal issue.

Kerr, of Glasgow, has observed a mortality of 20 per cent. in these patients with an infantile mortality of 95 per cent. Some cases had recovered with no other treatment than rest, the hemorrhage ceasing spontaneously. If the operator decided to rupture the membranes, he thought that a foot should be brought down in addition. In severe cases he believed that Cæsarean section was distinctly indicated.

Byers was also in favor of Cæsarean section in concealed accidental hemorrhage. Where the hemorrhage was external with absence of labor pains, he believed in the Rotunda method of tamponing. He called attention to statistics from the Rotunda of 56 cases where forcible delivery was employed in serious conditions with six deaths. In a second series of 57 cases where forcible delivery was not done but tamponing was used instead, there were but one death. In the last two reports from the Rotunda there were 34 cases without a death.

Nicholson had seen good results from dilating the cervix and emptying the uterus and especially with the use of bipolar version. He had seen good results from giving ergot, digitalis and quinine after delivery of these patients. He had seen after delivery continuous hemorrhage from the lower uterine segment. This was best treated by tamponing with iodoform gauze wrung out of adrenalin solution. The injection of saline solution was also useful in these cases.

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**Treatment of Birth Paralysis of the Upper Extremity by Suture of the Fifth and Sixth Cervical Nerves.**—In the *British Medical Journal*, October 22, 1904, Kennedy contributes further histories of cases of birth paralysis of the upper extremity treated by suture of the fifth and sixth nerves,

He believes that the lesion is caused by stretching the nerve cords. This is brought about when the shoulder is forcibly depressed and the head bent to the opposite side and rotated. In this position, the junction of the fifth and sixth nerve is under its greatest tension while the lowest cords are scarcely at all affected. This position may be brought about in any presentation by forcible traction, and hence this accident is independent of the fetal presentation.

On operation, the lesion found consisted of eicatrieial tissue making pressure and resulting from incomplete rupture of the nerve; rarely the eicatrieial tissue is found outside the nerve trunk and surrounding it. The operation consists in excising eicatrieial masses and suturing the nerve together. Before dividing the nerves, electrieal stimulus was applied and the loss of the conduction carefully ascertained. Meehanical stimulation may be used as desired and produces the same results.

The operation should be done as soon as possible after the receipt of the injury. It is well to wait two months with the hope of spontaneous recovery, testing the electrieal reactions during this time.

In cases where the lesion is an old one and electrical stimulation as ordinarily applied produces no result, the skin may be opened by a stab wound with a tenotome and a sterilized wire electrode passed directly downward to the muscle. In this way the reaction of the muscle may be accurately tested.

In eight cases in which operation was done, seven had been successful in various degrees. This accident occurred in the practice of competent obstetricians and was no evidence of carelessness or unskilful practice.

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## GYNECOLOGY.

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UNDER THE CHARGE OF  
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ASSISTED BY  
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**Ileus after Laparotomy.**—In a discussion on this subject before the Dresden Gynecological Society (*Zentralblatt für Gynäkologie*, No. 27, 1904), LEOPOLD stated that he had seldom met with this complication of late years, and attributed it to improved technique and more rapid operating. In the majority of cases it is due primarily to sepsis. As prophylactic measures he mentions complete control of oozing, protection of the intestines during operation, and a careful search for any possible imprisoned loop of gut before closing the cavity.

Peters stated that he gave no purgatives before operation, but only enemata, in order to disturb the intestines as little as possible.

Goldberg reported two successful and one fatal secondary operations for ileus, due to adhesion of a loop of gut. He cited a fourth case in which eleven (!) abdominal sections were performed for the



relief of intestinal obstruction which first developed nine years after the primary operation. As he expressed it, the peritoncum was literally in a condition of general granulation (*Ausgranulieren*.) Finally the gut was resected and an artificial anus was successfully established.

Wagner-Hohenlobese, in closing the discussion, contended that ileus was nearly always of inflammatory origin. He did not believe that the length of the incision had anything to do with the conditions.

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**Adrenalin in Gynecology**—PETERS (*Zentralblatt für Gynäkologie*, No. 27, 1904) uses a 1 : 2000 or 1 : 3000 solution of the drug on an applicator within the uterine cavity to control hemorrhage after curettement, especially in cases in which he proposes to introduce a 30 per cent. formalin solution as a caustic. He has also found it of value in cases of metrorrhagia, especially when combined with solutions of suprarenal capsule. He recommends it also in cases of chronic urethritis, but regards it as especially valuable in vulvitis and pruritus, even when quite acute. He applies solutions of from 1000 to 3000 to the vulva, allowing them to remain in contact with the parts from two to five minutes.

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**Cysts of the Spleen.**—MONNIER (*Beiträge zur Klin. Chirurgie*, Band xli., Heft 1) has been able to collect only 13 cases of non-parasitic cysts of the spleen, to which he adds another successful splenectomy from Krönlein's clinic. The condition is most common in women, and the etiology is obscure, trauma being a recognized cause. Multiple cysts of the spleen, as large as a pea or cherry, are common, but they seldom develop into large tumors. Their growth is slow, is attended with attacks of pain and vomiting, and later with pressure-symptoms. Changes in the blood are rarely observed. There is a temporary leukocytosis after operation. In the writer's case a peculiar perisplenic crepitus was felt. All the 14 cases terminated successfully, different measures being adopted—simple puncture, incision and drainage, enucleation, and splenectomy.

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**Aspirin in Obstetrics and Gynecology.**—GOTH (*Medizinische Blätter*, No. 6, 1904) reports 276 cases in which he found this drug a valuable analgesic, especially in dysmenorrhœa and inoperable carcinoma. He used it also successfully for the relief of painful uterine contractions after labor and curettement; 7 grains are administered every half hour until pain is relieved. If no effect is obtained after four doses have been given it is inferred that there is no use in continuing the drug. In cancer cases 15 grains are given at once. No unpleasant after-effects were observed in any instance.

[We have now under observation a case of recurrent cancer following hysterectomy in which 5 grains of aspirin always give prompt relief after codeine had been used in vain.—H. C. C.]

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**Thigenol in Gynecology.**—NAUMANN (*Deutsche Ärzte-zeitung*, Heft 19) has tried this sulphur compound in 100 cases, as a substitute for ichthyol, and finds that it is not only a more powerful local analgesic but is free from odor and does not soil the patient's linen. He uses it in metritis, erosions of the cervix, enlargements of the adnexa, and pelvic exudates, also in acute urethritis.

**Cystitis after Gynecological Operations.**—BAISCH (*Beiträge zur Geburtshilfe und Gynäkologie*, Band viii., Heft 2) reports 40 cases which were examined bacteriologically on the first day of their inception. He found streptococci in six specimens of urine, staphylococci in 34, and in 10 colon bacilli in addition to the two former. The latter were never found in any urine before operation, but in cystitis persisted as late as the third or fourth week. He concludes that post-operative cystitis is due to primary staphylococcus or streptococcus infection, with subsequent infection with the colon bacillus. Repeated examinations of the urethra, vestibular region and vulva convinced the writer that the infection always comes from without, and usually through catheterization. He recommends that every effort be made to induce the patient to void her urine spontaneously after. To this end he injects half an ounce of sterilized boroglycerin into the full bladder on the evening following the operation. This generally causes the patient to urinate within the course of five minutes. If it is absolutely necessary to use a catheter, as soon as the bladder is emptied he injects 500 c.c. of a 3 per cent. solution of boric acid. In this way he believes that it is possible to practically eliminate post-operative cystitis.

Rosenstein (*Zentralblatt für Gynäkologie*, No. 28, 1904), in commenting upon Baisch's paper, thinks that "prevention is better than cure." He reports the results of his observations in Israel's clinic, where, by using a double catheter, devised by himself, a series of 34 cases were catheterized with only a single case of cystitis. The instrument consists of an outer tube which is introduced only as far as the urethral sphincter, when the catheter proper is pushed through it into the bladder, without coming in contact with the external genitals.

**Ectopic Gestation Associated with Acute Suppuration.**—HITSCHMANN (*Zentralblatt für Gynäkologie*, No. 27, 1904) reports a case of ruptured ectopic (at the isthmus) in which the portion of the tube between the uterus and the ovum was filled with pus containing gonococci. The outer two-thirds of the tube were perfectly normal. The writer infers that the acute inflammatory process resulted from the closure of the tube preceding the development of the ectopic, and proves that nidation is not prevented by a purulent condition of the mucosa.

**Malignancy of Ovarian Cysts.**—In a discussion on this subject before the French Congress of Obstetrics and Gynecology (*Annales de Gynécologie et de Obstétrique*, July, 1904) CERNÉ stated his conclusions as follows: 1. Any ovarian cyst may become malignant. 2. There is no authentic case of recurrence after the removal of a paucilocular cystoma containing fluid of low specific gravity and lined by typical epithelium. 3. All other varieties may recur after removal, the papillary being most prone to metastasis. 4. However, cures have often followed the extirpation of papillary cysts, even when the peritoneum was involved. 5. At least one-fourth of these cases are really malignant, and terminate fatally.

Lejars, in continuing the discussion, stated that in his experience 15 per cent. of all cases of cystoma were malignant. Ascites was always a suspicious symptom, and he regarded bilateral cysts as so doubtful as always to justify hysterectomy.

Pozzi disagreed with the first speaker in believing that a large proportion of papillary cysts were benign. Implantation of papillary growths on the adjacent peritoneum should be carefully distinguished from true lymphatic metastasis, since the former was far from being an evidence of malignancy. A certain number of cysts undergo true cancerous degeneration, but this change is usually circumscribed at the outset, and cannot be positively determined at the operating-table. He concludes that in the absence of true metastasis and cachexia the surgeon should proceed as in an ordinary ovariectomy. Both ovaries should be removed if one shows only commencing papillary degeneration, especially if the patient is near the menopause, and hysterectomy is also usually indicated. Drainage is always indicated in the presence of ascites(?). Even in an inoperable case an explorative incision is often beneficial.

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## OTOLOGY.

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UNDER THE CHARGE OF

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**Local Anæsthesia of the External Auditory Canal and Middle Ear.**  
—VON EICKEN (*Verhandlungen der Deutschen Otol. Gesell.*, Berlin, May 21, 1904) states that infiltration anæsthesia is impracticable on account of the tense union between the skin and the cartilage or bone. The freezing method as well as the application of solutions of anæsthesin have given no telling results.

Brauns showed the possibility of doing major operations by injecting a weak solution of cocaine with a trace of adrenalin in the neighborhood of the corresponding nerve roots to the part operated on.

The ramus auriculotemporalis nerve innervates the posterior wall of the auditory canal and a branch of the auriculotemporalis innervates the anterior wall. These nerves enter at the junction of the fibro-cartilaginous and osseous portions of the canal and send branches to the drum membrane.

The ramus auricularis enters the tympanomastoid fissure, therefore, very near the body surface, and is best injected in the posterior fold of the auricle slightly above the tip of the mastoid, inward and somewhat backward. The canal branch of the auriculotemporal nerve is best injected with the patient's mouth wide open, the needle being carried in a direction parallel to the anterior wall of the canal and the injection made at a point 2 cm. from the tragus. In children the distance inward is somewhat less.

The point of injection may be made painless by freezing with ethyl-chloride and by injecting a small quantity of the fluid at the moment

of introduction of the needle. There is no danger of harming the facial nerve.

Von Eicken injected 1 c.c. of  $\frac{1}{2}$  per cent. solution of cocaine, to which was added 2 drops of adrenalin, and after a few minutes the external auditory canal became completely anæsthetic. Complete anæsthetization of the drum membrane was not effected because the tympanal side of the drum is innervated from the carotidotympanicus plexus.

It takes a few minutes for the cocaine to act, the adrenalin causing the maximum contraction of the vessels and acting like a ligature. By using so small an amount of cocaine as 5 mg. intoxication in the adult is practically avoided, but with children even less should be used.

This method has thus far been used only in cases of furunculosis of the canal, it being possible to make broad openings and curette them without causing pain. Von Eicken has not yet experimented with exostoses and new-growths.

This method is especially useful in cases of foreign bodies difficult of extraction, and as a substitute for general narcosis and the laying free of the canal wall from behind.

Von Eicken hopes ultimately to be able to incise the drum-head painlessly under this local anæsthesia, and is experimenting in that direction.

At the Heidelberg clinic the drum-head is made anæsthetic before incision by means of a 40 per cent. solution of cocaine which is left in contact for some time, and, in cases where a perforation of Schrapnell's membranc exists, the tympanic cavity is made anæsthetic by application of cotton sticks soaked with 40 per cent. solution of cocaine, and hammer-incus extraction is easily and painlessly done without general narcosis.

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**Thiosinamine Treatment of Chronic Middle-ear Catarrh.**—MARTIN SUGAR (*Arch. f. Ohrenh.*, Bd. lxii., H. 3 u. 4, S. 241). In this paper the author quotes Grunnert as saying that the pathological anatomy of sclerosis unquestionably points the way to internal treatment of chronic middle-ear catarrh.

The chemical formula of thiosinamine, the value of which in the treatment of lupus was first shown by Hebra in 1892, is  $CS < \begin{smallmatrix} NHC_2H_5 \\ NH_2 \end{smallmatrix}$  and is obtained by warming an alcoholic mustard solution with  $NH_3$  at  $100^\circ$  under pressure. It is colorless, bitter-tasting, odorless in a pure state, soluble in water, and especially so in alcohol and ether.

After giving a *résumé* of its uses in general medicine, Sugar tells of his experience in its use in treatment of the ear. He used it subcutaneously and also in a 10 per cent. glycerin-water solution, 5 or 6 drops of which were blown into the tympanic cavity through the catheter. Sugar thinks its worth is clear in cases of hindered or abolished function of the fenestræ of the middle-ear cavity, what Panse called in his monograph "difficult hearing through rigidity of the middle-ear fenestræ," whether brought about through rigidity of the stapes, through adhesions or rigidity of the annular ligament, or independent rigidity of the round window, or disease of both windows, or hammer and incus fixation, that is, ankylosis of their joints, so long as they had not come to ossification. Furthermore, the treatment appears to be applicable

to cases of cloudiness of the drum-head; beginning calcification and thickening of the drum-membrane; in thickening and fibrillary connective-tissue changes in the mucous membrane of the middle ear; in new-formed connective-tissue membrane and ligaments which cause abnormal union of parts of the sound-conducting apparatus; in connective-tissue atrophy of the ligament of the tensor tympani muscle, thereby causing partial retraction of the drum-membrane; in connective-tissue changes of the stapedius muscle without atrophy, and in arthritic processes of the joints of the ossicles. In cases where there is osteoporosis of the labyrinth capsule the thiosinamine treatment has not proved of service.

Thiosinamine is likewise indicated in cases of narrowing of the tympanopharyngeal tube through rhinoscleroma and also in cases of keloid of the lobule; the drug also acts on scar tissue and adhesions left after chronic suppurative otitis.

In two cases of middle-ear catarrh Sugar inflated five to six drops of the glycerin-water solution daily into the middle ear. In one case in which the drum-membrane was adherent it became movable after three weeks' treatment, the hearing improved, and the subjective disturbances decreased.

Small amounts of a 15 per cent. alcoholic solution were also injected into the mastoid region and larger amounts into the arm without harm or discomfort other than a slight burning at the point of injection. The 10 per cent. glycerin-water solution has the disadvantage that it precipitates on standing and must be warmed before using.

Thiosinamine is indicated, outside of catheter treatment, in the early stages of otosclerosis in young patients without hereditary taints, and in syphilitic middle-ear disease where pilocarpine has often been used without results; it should not be used in the course of an inflammatory process.

That connective-tissue adhesions actually become changed by thiosinamine cannot, after the histological findings of Glas, be doubted, and all writers on this subject speak of the elective affinity of thiosinamine for scar tissue, but only by further experimentation can the exact value of this drug be determined.

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#### Manifestations of Traumatic Hysteria in the Organ of Hearing.—

DR. ERNEST BARTH (*Archives of Otology*, December, 1904) reports two interesting cases of hysterical deafness, the first in a young girl, aged eleven years, who was frightened by a dog leaping suddenly upon her in the dark. She was able to relate, in a stammering voice, what had happened to her, but soon lost her speech and moved her arms convulsively. On the following day she had apparently entirely recovered, but there was a complete bilateral deafness, which disappeared eight days later without treatment, but recurred when, a week later, she was startled in the dark by the sudden appearance of a friend. In this second attack the deafness was complete to all tests, but musical sounds were unconsciously heard, and at the end of two weeks the general hearing was again normal.

The second case was that of a man, aged twenty-one years, who, a few hours after attempting to dive, felt blood oozing from the left ear, and on the following day noticed an impairment of hearing in the same ear. Examination of the ear showed nothing abnormal, with exception

of a small cicatrix in the drumhead and a sensitiveness on pressure at the tip of the left mastoid process. The whispered voice was not heard in either ear, and the spoken voice only close to the right ear. The tuning-fork was not heard by bone conduction upon either side, and by air conduction on the right side only. There was tinnitus, which disappeared at the end of two days. The tactile sense of the integument of the left external auditory meatus and the left drumhead was normal, but the entire left half of the body was hyperæsthetic, and convulsive movements were noticeable in different groups of muscles.

The sensory paralysis gradually increased, and after ten days the entire left half of the body had become anæsthetic. The temperature sense was also lost. There was anosmia, and the oral, pharyngeal, laryngeal, and nasal mucous membranes were insensitive to touch. The sense of taste on the left side of the tongue was wanting, but remained normal on the right side. Ophthalmoscopic examination showed the fundi to be normal, but the visual field was decreased in both eyes, and the conjunctiva less than normally sensitive. Under careful observation of the succeeding symptoms it was found that while the tactile sense of the left external ear and the canal was wanting and the ear apparently totally deaf to sounds aërially conveyed and by bone conduction, the mastoid region was hyperæsthetic. With the right ear tightly closed the patient would sing accurately a note struck upon a piano, and would, moreover, sing five or six notes in musical sequence.

This condition remained unchanged for months, with the addition of certain morbid feelings, treatment, including hypnotism and metallotherapy, were of no avail. Ten weeks after the onset of the disease the patient had total night blindness, and had to be led about after sundown, and there was marked decrease in sight, minus glasses bringing the vision up to 6/15 of normal only.

Barth believes the cause of this curious train of symptoms to have been mental entirely, the exciting cause being the impression made by the oozing of the few drops of blood from the ear, there being no inflammatory symptoms to account for the persistent tenderness of the mastoid process.

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## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

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UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,  
OF PHILADELPHIA.

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**Primary Malignant Endotracheal Tumor.**—DRS. JUDSON DALAND and JOSEPH MCFARLAND present a preliminary report with illustrations, macroscopic and microscopic (*Journal of the American Medical Association*, September 3, 1904) of a case of primary malignant endotracheal tumor in a woman, aged thirty-four years, as detected at the autopsy ten hours after death from suffocation and exhaustion, seven

months after the onset of cough followed by dyspnoea and expectoration. A papillomatous tumor about the size of the distal phalanx of an adult finger was discovered at or about the lower third of the anterior wall of the trachea, extending almost to the bifurcation, measuring  $5 \times 3\frac{1}{2}$  cm., and occupying more than three-fourths of the calibre of the tube. Immediately beneath this growth were a few moderately enlarged glands about the size of a marrowfat pea, which were firmly adherent to the outer wall of the windpipe at a region corresponding to the place where the innominate artery comes in close relation with the trachea, at which point the recurrent laryngeal nerve was compressed by the enlarged glands and inflammatory exudate.

As a result of the microscopic examination, the situation of the tumor, the peculiarity of the cells of which it was composed, the partial cornification of the cells, it was suggested that the tumor had developed from an inclusion of an œsophageal epithelium in the wall of the trachea during embryonal life.

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**Adenocarcinoma Occupying all of the Sinuses, Nose, and Orbits.**—At the recent meeting of the American Laryngological, Rhinological, and Otological Society, held in Chicago, May 30 to June 1, 1904 (*American Medicine*, July 2, 1904), DR. WILLIAM H. DUDLEY, of Easton, Pa., read a paper and presented a pathological specimen from a patient, aged sixty-three years, who had undergone a number of operations for growths in the nose, rhinopharynx, maxillary sinus, and orbit, continuing to involve one sinus after another until the whole anterior portion of the head had become one mass of adenocarcinomatous tissue. An examination of the bisected specimen showed practically none of the osseous framework of the head, except the sphenoid and frontal bones; and a portion of these was also absorbed.

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**Nasal Obstruction as Cause of Deafness without Other Disease of the Hearing Apparatus.**—DR. WALLACE MACKENZIE, of Wellington, N. Z., reports (*Journal of Laryngology, Rhinology, and Otology*, June, 1904) a case of a healthy man, aged twenty-four years, who became deaf after having his nose treated with electric cautery for difficulty in breathing.

Dr. Mackenzie found both nasal passages closed by adhesion of the external walls to the septum. Under chloroform he separated the adhesions with a probe-pointed bistoury, and prevented readhesions by the insertion of a long slip of celluloid from a photographic film. Healing took place readily, and the patency of the passages was soon re-established.

A fortnight after the operation hearing was distinctly better, the improvement having been noticed suddenly. Tests with the tuning-fork, whistle, watch, and spoken voice showed the hearing distance to be up to the average, and the range of hearing to be good.

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**Tuberculosis of the Tonsils.**—In a paper upon "The Significance of Tuberculous Deposits in the Tonsils," read at the late meeting of the American Medical Association, DR. GEORGE B. WOOD, of Philadelphia (*American Medicine*, June 11, 1904), expressed his opinion as the result of an exhaustive study involving much original research that tuberculosis of the tonsils occurs secondarily with almost every advanced case

of pulmonary involvement, and that it occurs as a primary infection in about 5 per cent. of all hyperplastic, faucial, and pharyngeal tonsils.

**Recurrent Papilloma of the Larynx of Forty Years' Duration.**—At the recent meeting of the American Laryngological, Rhinological, and Otological Society, held in Chicago, Ill., May 30 to June 1, Dr. WILLIAM L. CULBERT, of New York, reported a case (*American Medicine*, July 9, 1904) of a lady from whose larynx in 1864 an amount of tissue equal in bulk to a small hen's egg was removed endolaryngeally by the late Dr. Elsberg. Recurrence required subsequent removal after access by thyrotomy. Aphonia and dyspnoea of the patient were completely relieved, and remained absent for more than twenty years, when a return of the growth was apparent, and the patient came under the care of the late Dr. Rufus Lincoln, who removed the ever-recurring growth many times during the next ten years. After two or three years of comparative freedom from symptoms the patient came to Dr. Culbert in a desperate condition from dyspnoea due to a papillomatous growth covering the entire larynx with the exception of a small opening of about the circumference of a thin lead pencil. The growth was attached by a broad base throughout the right and upper parts of the larynx, to the epiglottis, and to a lesser extent of the right side of the larynx. These recent growths were removed with cutting ring-forceps in a number of sittings, and were papillomas, pure and simple. Restoration of voice and free respiration were secured, but the growth increased in size when let alone.

## PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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**Cytology of Pleural Effusions.**—VARGAS-SUAREZ (*Beiträge zur klinik der Tuberkulose*, 1904, Band ii., p. 201) discusses the origin and significance of the cells found in pleural effusions. He advises the May-Grünwald method of fixation and staining, but if thin smears are made from a specimen of the exudate, centrifugalized before clotting has occurred, Wright's method of staining gives excellent results.

The author discusses the various theories held as to the production of the true lymphocytosis and the formation of pseudolymphocytes in exudates, and reviews the literature as to the diagnostic value of the cells. He reports his cytological findings in fifteen so-called idiopathic pleurisy, where lymphocytes were in large excess; two cases, one of tuberculous, the other of rheumatic origin, which were nearly free from cell elements, and two cases of mechanical effusion, where endothelial



cells often in "placards" were seen in numbers. He also reports cases where an increased proportion of eosinophiles was found, one being general carcinosis, in the exudate of which cancer cells were present; and two being of obscure origin, where there was an eosinophilia in the blood. In two instances the author was able to make a certain diagnosis of carcinoma by the discovery of tumor cells in the exudate. From his own work and the review of the literature he draws the following conclusions:

The majority of the lymphocytes occurring in pleural effusions are true lymphocytes, derived by active migration from the blood of lymph vessels. They are not degeneration products of endothelial cells, nor are they lymphoid cells derived from the fixed tissues.

A small part of the lymphocytes are derived by the dividing of polymorphonuclear leukocytes, the so-called pseudolymphocytes being thus formed. A predominance of lymphocytes in pleural effusions is characteristic of the mild inflammations of the pleura. This has nothing to do at all with the lack of fluid of the tissues, as Neuman considered, but is dependent upon a mild irritation which calls forth a lymphocytic exudate. Since such slight irritations of the pleura are generally due to tuberculosis, the lymphocytosis of the exudate forms a strong argument for the assumption of a tuberculous infection. The presence of numerous endothelial cells in the exudate indicates that affection of the pleura is not of an inflammatory nature, and numerous polymorphonuclear leukocytes establish the fact that there is an inflammation of the pleura due to a more or less violent infection. In primary tuberculous pleurisy polymorphonuclear leukocytes are found in numbers only in very early cases or in mixed infections (empyema).

Eosinophiles in the pleural exudate are probably not called forth by infection, but stand in association with dyspnoea, and the presence of endothelial cells in the exudate. There usually exists simultaneously an eosinophilia in the blood.

With the help of a study of the cells in the exudate a diagnosis of new growth of the pleura or peritoneum can sometimes be made with surety by finding some of the cellular elements derived from a malignant growth.

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**Observations upon Natural and Artificially Produced Leukotoxins.**  
—CHRISTIAN (*Deut. Arch. f. klin. Med.*, 1904, Band lxxx., p. 333) gives the details of certain experiments with leukotoxins. The presence of the leukotoxins in the serum was determined by treating the blood of one animal with the serum of another animal, and observing the effect upon the movements of the leukocytes under the microscope. No differentiation was made between the different cell forms of the white blood corpuscles. As compared with natural hæmolysins, natural leukotoxins were exceedingly rare. The only serum that possessed natural leukotoxic properties was that of the chicken, which was active for the leukocyte of the dog. Artificial leukotoxins for the white blood corpuscle of the rat were produced in the serum of the guinea-pig by injections of rats' spleen.

Although the motion of the leukocytes was stopped, solution did not take place. Further experiments showed that leukotoxins could also be produced by the injections of various organs which had previously been washed free of blood. The author, therefore, concludes that

leukotoxic serum is not specific, inasmuch as it can be obtained artificially by injections of organs other than those which are concerned in the formation of blood cells. The leukotoxin, like the hæmolysins, is destroyed by heating at 55° C. for one-half hour.

**Soluble Toxins of the Typhoid Bacillus.**—LAGRIFFOUL and WAHBY (*Central. f. Bakt. u. Parasitkunde.*, Original, 1904, Bd. xxxv. p. 593) have succeeded in obtaining a substance in filtered cultures of the typhoid bacillus, which shows mild toxic properties for animals when injected intravenously or intraperitoneally. This toxic product varies in amount according to the conditions under which the organisms are grown. It is only present in any amount in young cultures, and if the growth is prolonged the toxin disappears. These facts are offered as an explanation for the failure of other observers to obtain a similar toxin in filtered cultures. The toxic substance is precipitated by alcohol and destroyed at temperatures of 52° to 58° C. The bodies of the typhoid bacilli from these cultures were killed by thymol and subsequently washed in salt solution. After suspension in salt solution these emulsions were injected into animals in doses corresponding to the amount of filtrate used. It was found that the bodies of the dead bacilli were less toxic than the filtered cultures. Further studies went to show that the toxicity of the filtrate was due to an elaboration of toxin by the living organism and did not result from the liberation of an intracellular toxin from the bodies of dead bacilli which might be present in the cultures. The authors conclude that living typhoid bacilli are capable of producing at least small quantities of a soluble toxin when grown in artificial culture media.

**The Results of Obliteration of the Pyramids of the Kidneys in Rabbits.**—TOLLENS (*Virch. Arch.*, 1904, Bd. clxxvii. p. 477) succeeded in closing the outlet from single medullary pyramids in the kidneys of rabbits and made observations on the changes which took place after intervals of four, eight and one-half, and twelve weeks. After four weeks the tubules of the medulla and cortex which had been drained by the occluded papilla showed a general dilatation, while a new formation of connective tissue could be observed in the cortex. After eight and one-half weeks the lesions had progressed in two directions. Some of the closed tubules had reopened and returned to their normal size. Elsewhere there had been marked increase in connective tissue, with compression of certain groups of tubules. Finally, a few canals, principally in the cortex, showed extreme distension. After twelve weeks the areas changed to small, contracted, well circumscribed scar-like masses, which had much the appearance of the contracted kidney. Microscopic examination showed that the areas were made up of dense connective tissue, with here and there a few remnants of tubular epithelium. These changes are analogous to the alterations produced in other organs after the closure of their excretory ducts.

**The Pathological Effects of Periodic Losses of Blood.**—The regular and periodic abstraction of blood from horses which have been used for the purpose of producing antitoxins leads to certain cases to serious derangement and death. A preliminary survey of these observations suggested to Theobald Smith (*Journal of Medical Research*, 1904, vol.

xii., p. 385) that the phenomenon which controlled the pathology of the condition was hæmolysis due to a weakening of the red cells. To test this hypothesis the resistance of the red cells of normal horses and of horses which had been repeatedly bled was determined toward various percentages of salt solution. With the red blood corpuscles of the normal horse hæmolysis begins when 0.60 per cent. salt solution is used and is complete with 0.42 per cent. solutions. These figures represent the maximum and minimum resistance of the blood cells. The resistance of the red corpuscles of most of the horses which had been repeatedly bled was so changed as to correspond to a rise in osmotic tension of 0.04 to 0.09 per cent. salt solution. Whereas, in the normal horse the greatest number of corpuscles are destroyed with solutions of 0.48 to 0.50 per cent., in the horses which have been bled, the most pronounced destruction may take place with 0.56 to 0.58 per cent. solutions. There is no evidence at hand to show that the injections of diphtheria toxin play any appreciable part in this change. Further experiments showed that the osmotic tension of the serum does not adapt itself to the change in the corpuscles.

**Investigation upon the Anopheles in Hibernation.**—SUZUKI (*Sei-I-Kwai Medical Journal*, 1904, xxiii., p. 81) finds that the anopheles mosquito may hibernate during the winter, and indeed is able to exist at a temperature of 7° C. Though the vital functions of these mosquitoes are much reduced, still the insects are capable of slow motion, and may even fly when disturbed. Between January 20th and April 1st the author was able to collect 186 mosquitoes, all of them females. During hibernation the insects do not retain that peculiar position which distinguishes them in summer, but rest like culex, with the axis of the body parallel to the wall. Most of the anopheles possessed fully-developed ovaries, and in a few instances ripe eggs were observed. The appetite of the insects is so slight that, as a rule, they are not likely to feed upon blood, though under favorable circumstances they may do so. In summer the digestion of the blood is completed in two to four days, whereas in winter the process is much slower and may take two weeks. On March 8th the author allowed himself to be bitten by several hibernating anopheles which had been kept in feeding cages. On March 24th symptoms of a quotidian malaria developed, while on April 1st a microscopic examination of his blood revealed great numbers of parasites. Without further investigations the author is not prepared to draw definite conclusions as to the origin of winter and spring malaria, but he inclines to the belief that the infection may be brought about by the bites of hibernating anopheles mosquitoes.

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A REVIEW OF ONE THOUSAND OPERATIONS FOR  
GALLSTONE DISEASE, WITH SPECIAL  
REFERENCE TO THE MORTALITY.<sup>1</sup>

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AND

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FROM June 24, 1891, to December 1, 1904, we had made 1000 operations upon the gall-bladder and bile passages, with 50 deaths (5 per cent.). About 95 per cent. of the cases were operated upon in St. Mary's Hospital and under nearly identical conditions.

In a rapidly growing field of this character there have necessarily been many changes in technique. For such improvements we are much indebted to the literature of the subject. We have benefited from the work of Murphy, Ochsner, Elliot, Richardson, Park, Bevan, McBurney, Halsted, and a host of others, and especially to the late W. E. B. Davis. To Robson, Moynihan, Kehr and Reidel, we wish also to acknowledge a debt of gratitude.

A study of mortality must be based upon some definite plan, and, so far as the writers know, there is no settled method upon which a correct estimate of the death rate in any series of operations can be compiled. What are we to understand by a mortality of a certain percentage? Some operators say that if a patient dies as a result of the operation itself, it should be counted; whereas, if the operation failed and the patient continued along for a time, then died from the disease or of a complication, it should not be charged to the operation. The defect in this method is that it allows of a large degree of personal equation, and the same statistics may be made to look very

<sup>1</sup> Read at the meeting of the Southern Surgical and Gynecological Association, by Charles H. Mayo, M.D., 1904.



well or very badly, as the critic is prejudiced for or against the operation. One very prominent operator declares that any individual dying within fourteen days from any cause should be attributed to the operation, and after that time it was a question to be settled by the judgment of the surgeon. In this series of cases we have taken the view of the layman, that if the patient goes into the hospital alive and comes out dead, the death resulted from (or in spite of) the operation. It is to be understood, therefore, that in estimating the death rate we have charged as a death from operation every patient who died in the hospital, without regard to cause of death or the time which elapsed between the operation and the fatal issue. It includes patients dying as long as three months after operation and from intercurrent disease or accidental cause, such as apoplexy, pneumonia, heart disease, chronic nephritis, etc. A percentage of the deaths could be fairly excluded, but as the object is to show the relative curability of gallstone disease rather than good statistics, we have concluded that the above method is at least unprejudiced. It undoubtedly has a tendency to exaggerate the dangers of operation, particularly in common-duct disease, where long-continued infections of the bile passages have resulted in blood changes, causing death at a late period. But it also illustrates the dangers of delay and the tendency to produce complications which operation may be unable to relieve.

In the 1000 operations there were 50 deaths in the hospital, or an average death rate of 5 per cent. In the benign series there were 960 cases with 4.27 per cent. For malignant disease, 9 deaths in 40 operations gives a mortality slightly in excess of 22 per cent.

Where the disease was limited to the gall-bladder, including all non-perforating infections, the mortality was 2.44 per cent.; 573 cholecystostomies, mortality 2.46 per cent.; 186 cholecystectomies, mortality 4.3 per cent. This does not include 101 cholecystostomies and 44 cholecystectomies performed as part of a common-duct operation. We have followed the rule of counting as one operation all the different procedures done through a single incision. The major or most serious is classified; the others are considered secondary and appear only in the record of the patient.

Of the common-duct operations there were 137 benign, with 16 deaths, 11.7 per cent. This gives a heavy mortality, but, as already pointed out, it is really a death rate of operation and disease, and means that 7 per cent. failed to recover from the direct results of the operation, that is, died within a few days; while 4 per cent. recovered from the operation, but did not regain sufficient strength to leave the hospital. Many cases operated were in desperate condition from prolonged icterus, anæmia, etc. No cases were refused operation if they so elected after a fair statement of the facts. Operations for malignant disease are discouraging; 40 operations, with 9 deaths in the hospital, and of those that recovered comparatively few received

sufficient palliation to repay the immediate risk, suffering, and expense. Two cases, however, can be considered favorable as to cure; both were instances of early carcinoma of the gall-bladder. In a few patients a thick-walled and functionally useless gall-bladder was removed, and examination showed malignant involvement, and in the 2 cases referred to no return has as yet taken place after more than two years. We have recently had 2 cases of a like character, but as yet too early to be considered as to the probability of cure.

Next to malignancy and acute perforative infections of the gall-bladder and pancreas, the most serious thing that can happen in gallstone disease is involvement of the common duct of the liver.

Contrast a mortality of 2.44 per cent. in 820 cases where the disease was confined to the gall-bladder with 11.7 per cent. in 137 cases where the common duct is involved.

It would exceed the limits of this paper to go into the details as to various operations performed, and we will confine ourselves to a short discussion of the mortality in the benign group of cases and a comparison of results after the three most common operative procedures, cholecystostomy, cholecystectomy, and choledocotomy.

It can be fairly stated that the average mortality of operations for diseases confined to the gall-bladder is not greater than for appendicitis in patients of the same age and condition of health. Gallstone disease is most frequent in people of advanced years—often obese and not infrequently the victim of some degenerative lesion of vital organs. One cannot directly contrast such cases with disease of the appendix, which is by far more common in younger and more robust subjects.

**CHOLECYSTOSTOMY.** Of these there were 573 (exclusive of 101 in connection with common-duct operations), with 14 deaths, a mortality of 2.46 per cent. This includes most of the acute infections with localized peritonitis. At least one-third of these deaths were from purely accidental causes that had to do with the general condition of the patient. The mortality of cholecystostomy in simple gallstone disease in otherwise normal individuals was less than 1 per cent. In 186 cholecystectomies (exclusive of 36 common-duct cases) the mortality was 4.30 per cent., or nearly twice that of cholecystostomies. It may be urged that this latter operation was elected in the more severe cases, and to a certain extent this is true, but not wholly so, as the more dangerous acute infections were nearly always drained by cholecystostomy. Inasmuch as in not a single instance did stones reform in the gall-bladder when left, cholecystostomy must be considered the safe operation, cholecystectomy being reserved for certain cases in which cholecystostomy may be expected to furnish, in a considerable proportion of cases, a partial or complete failure. Other things being equal, all cystic gall-bladders should be removed, and especially when a stone is impacted in the cystic duct, as not infrequently a stricture may follow removal, interfering with the

escape into the common duct of the normal secretions of the mucous membrane, thus giving rise to colics or external mucous fistula. As a rule, gall-bladders which are found to contain bile at the time of operation may be drained, as if bile can get through the cystic duct mucous secretion can escape. If the cystic duct should be considerably injured during removal of the calculus, introducing doubt as to the future permeability, the gall-bladder should, of course, be removed. Again, gall-bladders which are suspiciously thick and hard should be excised, as in this way early malignancy may occasionally be cured, as shown in the 2 cases referred to above.

In most cases of chronic cholecystitis without stones the gall-bladder should be removed. The presence of gallstones gives rise to irritation, and their removal, with subsequent drainage by cholecystostomy, may be expected to leave a harmless organ, but an infection which is able to continue without the aid of foreign bodies calls for a more radical operation.

We must not be too ready to diagnose cholecystitis without stones on operation, or we may cover a mistake in diagnosis, and send home an unrelieved patient with an unnecessary operation. Before a diagnosis of non-calculous cholecystitis is permissible, the duodenum, stomach, pancreas, appendix, and right kidney must be examined, and if the theory is correct the gall-bladder should be found thickened, of light color, with the lymphatic glands along the cystic and common ducts markedly enlarged. It should contain tarry bile and the mucous membrane should be not only thickened, but covered with little, fibrinous specks.

In patients who have gallstones and who have suffered from attacks of jaundice and other symptoms of infection of the common and liver ducts, but without stones in the ducts, cholecystostomy is the operation of choice, as it furnishes bile drainage. Cholecystectomy, if performed in this latter group, should not be accomplished by ligating the cystic duct, as it may be vital to secure bile drainage, and the duct must be left open, or, if necessary, split down to the common duct for this purpose. If the cystic duct is patulous, cholecystostomy furnishes this drainage easily and safely, and in case of future common-duct stone, the gall-bladder is a reliable guide to the common duct and greatly facilitates a secondary procedure.

It must be borne in mind that stones may form in the common duct secondary to an infection from gallstones in the gall-bladder, and especially so if a stone has passed through the common duct or has been removed from it. It has been urged that the gall-bladder in gallstone disease is obsolete and should be removed in every case. In our experience there has been a slightly increased hazard and without compensating increase in permanence of cure or shortening of convalescence in the average case. We find indication for removal of the gall-bladder in about 2 cases out of 5, but consider cholecystostomy the operation of choice, and only perform cholecystectomy

for definite pathological conditions, such as we have called attention to.

The most common cause of death where the gall-bladder alone was involved has been a descending infection of the common and hepatic ducts. Cholangitis, as a result of gallstone disease, at once introduces a most serious complication. As long as the stones were confined to the gall-bladder they were, so to speak, but a side issue to the possibilities of trouble engendered by lodgement in the deep ducts, for here an infection is lighted up which may extend to the smallest bile ducts, and over which, as compared with gall-bladder disease, we have but little control. A process is instituted which may result in stone formation, even in the most minute bile ducts, and future trouble after apparent cure may be the result. The death of 16 patients in 137 operations for gallstones in the common-duct series and 4 out of 9 malignant cases at once demonstrates the serious character of common-duct surgery. Not that the operation itself is particularly difficult nor prolonged, but we have two serious elements introduced, jaundice and infection, and the mortality, both immediate and remote, of choledochotomy depends almost entirely upon these factors. About one-third of all patients with common-duct stones have little or no jaundice at the time of operation and very little infection. However, at the time the stones passed into the common duct there will usually be found in the history that there had been both jaundice and infection, and during the acute stage operation would have been fraught with greater danger. During the quiescent period operation is very safe in such patients, and the mortality in our experience not more than 2 per cent.

Unfortunately, the majority of common-duct patients have either never had an intermission or have passed beyond it, and operation is no longer an election as to time, but a necessity, and, no matter how desperate, must be done to save life. In some cases the infection is the more prominent feature, giving typical ague symptoms. Sudden chills, with high temperature, followed by rapid decline, and a little temporary increase in jaundice and attended with moderate pain, and often nausea, are pathognomonic. In others there is little infection, but such a degree of bile stasis in the ducts as to invite infection after any kind of operation. Some individuals are almost sure to die. Patients with extreme jaundice and subcutaneous hemorrhage will nearly always bleed to death from capillary oozing. If purpuric spots exist with jaundice, we keep the subjects under treatment until the blood will at least remain in the proper channels. In all cases of jaundice we use chloride of calcium, following the advice of Robson for a few days before operation, but we are uncertain as to its exact value.

Another class of cases who have in our experience all died, and about whom we are not always able to foretell the conditions previous to operation, are those patients with obstructive jaundice in

whom no trace of bile is to be found in the bile passages, the common and hepatic ducts being filled with clear fluid. The liver has been put out of action. The patient, while extremely feeble, may be up and about. The jaundice is extreme, but is not necessarily accompanied by leaky bloodvessels and subcutaneous hemorrhages. We have had 4 of these cases, and all died within four days. In 2 cases a little bile appeared in the drainage at the end of twenty-four hours, but in none did liver action become re-established.

In a number of instances the same condition was met with at an earlier stage, the bile ducts being filled with thick, flocculent bile of a dark-greenish color, very much like that which occurs in the gall-bladder during the acute stage of cystic-duct obstruction and before the pigments have become absorbed. In about half of this group the liver will begin to functionate and the patient recover. In reviewing the deaths in common-duct operations, one is impressed by the influence of jaundice, not only in vitiating the general health of the patient, as shown in the tendency to capillary bleeding, but even more important in the invitation which it extends to infection. Combined jaundice and infection is the cause of most of the late deaths from general debility and exhaustion which occur after a primarily successful operation. While we have had no cases in which stones have reformed in the gall-bladder after cholecystostomy, we have had 2 cases in which stones formed in the common duct, after the removal of a single large stone from the gall-bladder in 1 case and in the other many stones from both gall-bladder and common duct, showing that stone formation may take place independently of the gall-bladder, but only when there have been primary stones in this viscus.

We have seen a number of cases of liver-duct stones, but there has always been a blocking common-duct stone from the gall-bladder at the papilla behind which the intrahepatic calculi had formed, the favorable condition of partial obstruction and mild infection furnishing the proper environment. In 2 cases we have had to operate a second time upon common-duct stones which had for their nucleus hepatic-duct stones which had drifted down into the common duct subsequent to the choledochotomy. In the 1000 operations, 14.6 per cent. involved the common duct.

## THE PSEUDOMALARIAL TYPES OF INFECTIVE ENDOCARDITIS.<sup>1</sup>

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CASES of infective endocarditis simulating malarial fever have been reported from time to time for half a century, yet adequate recognition has scarcely been given to the subject in text-books. Nor has the attempt been made, so far as I am aware, to bring together the various types. The importance of infective endocarditis and the difficulty often encountered in arriving at a correct diagnosis apparently justify a consideration of the pseudomalarial forms under which it may be masked.

Before the discovery of the malarial parasite, especially, the attempt was made to establish an etiological relation between malarial fever and infective endocarditis. It was entirely *post hoc* reasoning. Convincing proof of such relationship has not yet been offered. In fact, it is almost universally conceded that antecedent or coincident malaria is merely fortuitous. Some cases have given histories of recent or old-recurring malarial attacks, but these histories must be accepted with caution, at least in certain instances. The pseudomalarial types of endocarditis are subject to complete, though temporary, interruption for weeks at a time. Herzog has reported the coincident presence of the malarial parasite in one case, but does not prove its etiological significance. It was present also in a fatal case treated at Bellevue, and in another at City (Charity) Hospital.

The cases of infective endocarditis of pseudomalarial type which have been reported fall broadly into two groups, acute and chronic. The duration of the acute cases is measured by weeks, of the chronic by months. It will often be found, however, that cases which have died after a few weeks' observation give histories extending over several months. Other chronic cases may continue for eighteen months or more.

The pseudomalarial must be distinguished from the frankly septic and pyæmic forms of infective endocarditis, of which they constitute a remarkable sub-group. They differ rather in the periodicity than in the nature of the paroxysms. Their resemblance to malarial fever is often very exact. The paroxysms may recur at regular periods, even at the same hour, and the intervals be fever-free. In the apyrexial periods the temperature is often subnormal. No special infective agent is responsible for the pseudomalarial types, nor is it necessary that there shall have been previous cardiac valvular disease.

<sup>1</sup> Read before the Section on Medicine, New York Academy of Medicine, October 18, 1904.

The cause of the periodicity has not been determined. It has been thought to be due to disturbance of the heat-regulating mechanism by an antecedent malaria, and that the stamp of malaria is carried by the subsequent febrile movement. This seems unlikely, since no other febrile disease, when it follows a malarial attack, pursues such a course. Nor has it even been proved that the majority of cases have been recently preceded by malaria. Sicard found staphylococci in the blood in the pyrexial but not in the apyrexial periods of one case.

The following pseudomalarial types have been reported:

1. Double quotidian.
2. Quotidian.
3. Tertian.
4. Quartan.
5. Septan.
6. Mixed types.
7. Irregular.

A single case may present during its course several of these types, yet at a particular period each type be pure. It is almost characteristic of these cases that they change their course. In spite of this fact, it is advisable to speak of distinct types. Cases may be under observation for short periods only, during which a definite type is preserved.

When the disease is approaching a fatal termination, the paroxysms often return irregularly.

**CHARACTERS OF THE PAROXYSMS.** The paroxysms may be identical with those of malarial fever, presenting cold, hot, and sweating stages, with fever-free intervals. The cold stage may be accompanied by a prolonged, hard chill, or simply by sensations of chilliness. As in malaria, the temperature may rise steadily through the chill. The chills begin with or after the initial rise of temperature, which, though sharp, may occupy several hours in reaching its maximum. In acute cases the maximum is often very high, even  $107^{\circ}$ . The defervescence is sudden and generally marked. The temperature may fall  $1^{\circ}$  or  $2^{\circ}$  below normal. Subnormal interval temperatures have occurred in a number of cases. Sweating may be profuse, scanty, or absent. It is commonly present. Vomiting often accompanies a paroxysm. A single paroxysm may occupy from six to eight hours. The intervals between the paroxysms may be fever-free or show a slight-febrile movement.

*The Onset.* The onset is often like a simple malarial attack. The type may be established at once, or only after a period of irregular paroxysms. When first seen the patient may give a history of recent apparent malaria, with apparent relief from quinine. Such a history almost necessarily deceives one at first as to the true nature of the illness. It has probably led also to the false assumption of recent malarial attacks by some authors.

1. DOUBLE QUOTIDIAN TYPE.—I have been able to find only one case in which this type was followed unchanged to the fatal termination. The double quotidian type has generally appeared only toward the end of the disease. The previous course may have been quotidian, tertian, or irregular.

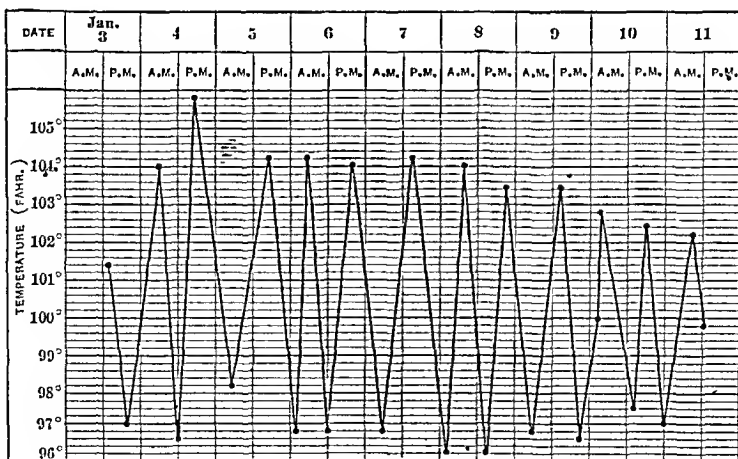
*Illustrative Case.* Coupland's Case I. Male, aged forty-one years. Gonorrhœa at twenty, otherwise healthy. Took cold two months ago. Next day had pain in left leg, which was relieved by local applications. Patient always felt weak afterward. Five weeks ago began to suffer from "shivering fits," from which he has not since been free. Paroxysms at irregular intervals, some every third day, some every fifteen hours. Thought he had ague. Each attack was accompanied by vomiting and was followed by an intolerable sense of heat. Became progressively weaker. No pain, but noticed latterly that legs swelled toward night.

*Status Præsens.* Looks very ill; is spare and sallow. Lungs practically normal. Cardiac dulness normal. Rough systolic bruit at apex. No thrill. Pulmonic second sound ringing; aortic dull.

*Course.* Throughout whole course, pyrexial periods averaged about five hours. Rigors, which sometimes commenced with and sometimes after the initial rise of temperature, averaged one and one-half hours' duration. The apyrexial periods, during which the temperature frequently fell to extreme subnormal levels, averaged ten hours. Absence of sweating was a marked feature.

Fig. 1 represents the double quotidian paroxysms. Fig. 2 represents double quotidian changing into quotidian paroxysms.

FIG. 1.



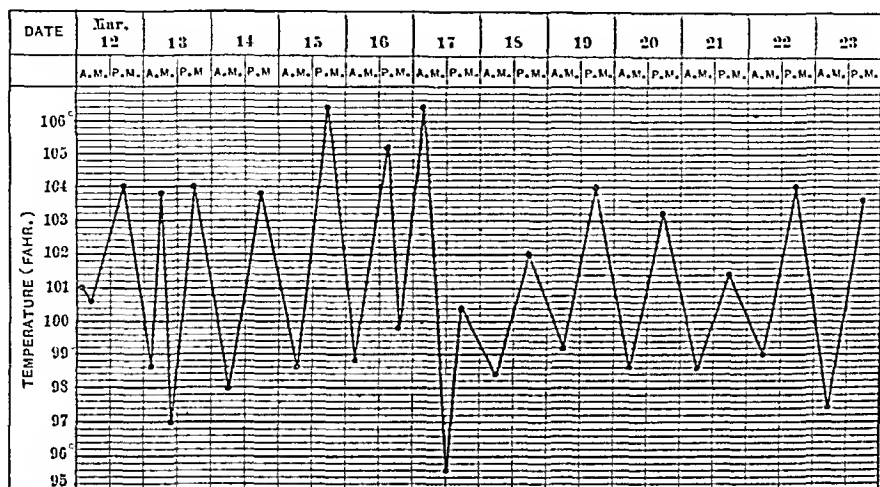
Double quotidian type. Coupland's Case I.

2. QUOTIDIAN TYPE. *Illustrative Cases.* Dock's Case I. (1895). Female, aged twenty-six years. Forceps delivery, with laceration



of perineum. Wound healed quickly. Three weeks later went sleighing. Afterward remained in bed. Had chills, fever, and sweating almost every day.

FIG. 2.



Double quotidian changing to quotidian. Coupland's Case II.

*Status Præsens.* Slight emaciation. Moderate effusion in right knee. Feet painful, but not swollen. Fugitive painful swellings in fingers. Heart enlarged, impulse heaving, loud mitral systolic murmur. Second sounds normal. No cardiac lesion found at examination prior to administration of chloroform for forceps delivery.

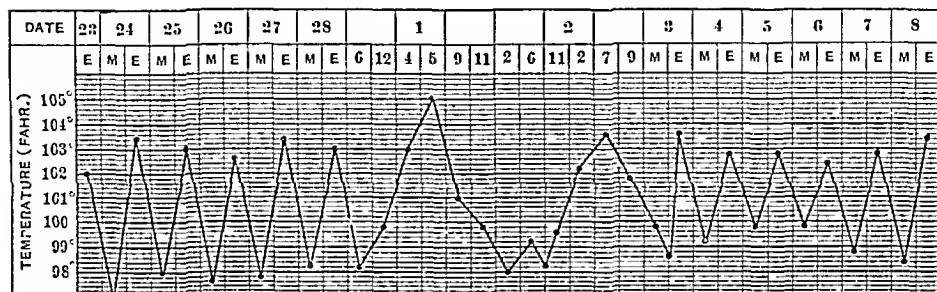
*Course.* Rise of temperature usually occurred about noon, reached its acme about 5 P.M., sometimes one or two hours later, and after remaining at about the same point for one or two hours fell rapidly, usually reaching normal by midnight. Toward the last subnormal temperatures often occurred. Chills not constant, though very common, coming on early in the rise of temperature and of short duration. Sweating almost always present in the decline. Patient felt well, though weak, during apyrexial periods. Pain in the knees, ankles, feet, and hands, and itching of the skin were frequent. No cutaneous hemorrhages, but urine became bloody shortly before death. Fig. 3 shows the quotidian paroxysms.

Osler has reported two remarkable chronic cases of quotidian type of ten and eleven months' duration.

Osler's Case I. Male, aged forty-three years. Indefinite history of chronic malaria when a young man. Illness began with a chill, followed by fever, malaise, and muscular soreness. Headache, loss of appetite, insomnia, and cough were marked symptoms. Spleen large. Symptoms abated in a few days and patient resumed business. Three weeks later marked dyspnoea, with increasing cough,

developed, and a loud systolic murmur was heard at the apex for the first time. Had daily intermittent fever, usually subnormal in the morning, and ranging from  $102^{\circ}$  to  $103^{\circ}$  in the evening, with occasional sweats. Pains in different parts of the body, particularly in the left inguinal region; tenderness over the fourth and fifth left costal cartilages. Fever continued throughout winter, with weakness, cough, and dyspnoea. Patient in the Johns Hopkins Hospital

FIG. 3.



Quotidian type. Dock's Case I. (1895). Portion of chart.

from March 15th to May 10th. There were no chills, only slightly chilly feelings. Morning temperature was  $97.5^{\circ}$  to  $98^{\circ}$ , with a gradual rise to  $102^{\circ}$  to  $103^{\circ}$  at 4 P.M., and a gradual fall to normal at midnight. Between 4 and 5 o'clock in the afternoon, sometimes not until evening, there was sweating, occasionally profuse; more frequently the skin was only slightly moist. The general condition improved somewhat, and the patient gained slightly in weight. The only complaint was pain in the splenic region, sometimes with very distinct tenderness. There was no change in the cardiac condition while in the hospital. The temperature range was low, and often subnormal toward the end. Petechiæ appeared. Sweating continued. The patient failed progressively. Diarrhoea developed. The urine contained blood and blood casts. Death.

3. TERTIAN TYPE. *Illustrative Case.* Elsner's Case I. Symptoms of intestinal infection for several days. At the same time had a persistent gonorrhœal discharge. Without marked disturbances of any kind, without evidences of constitutional infection, patient suddenly developed a tertian form of intermittent fever, and ague was suspected. It became evident after the third day that the prostration was greater than in malaria, the delirium more marked, and nervous symptoms more profound. There was increasing shortness of breath. Heart rapid, sounds suggestive of mitral insufficiency. Spleen large. Albuminuria. After the third chill, in spite of the fact that the tertian type of fever persisted, the temperature was always slightly elevated. Physical signs of auriculoventricular insufficiency, with aortic stenosis. Death in fourth week, in typhoid

condition, with hemiplegia, occasional chills, and sharp rises of temperature. Fig. 4 shows tertian paroxysms.

4. QUARTAN TYPE. *Illustrative Case.* Wenckelbach. Male, aged fifteen years. Entered eye clinic, after measles, for interstitial keratitis. Developed intermittent fever, complained of palpitation. Heart enlarged; sounds clear, but accentuated. Fever followed quartan type. Intervals not fever-free. No malarial parasites in blood. Daily attacks of palpitation, up to 160 per minute. Heart still further enlarged. Spleen enlarged, with piercing pains. Staphylococcus albus obtained from blood. Diagnosis, infective endocarditis. Cured after injections of collargol. Fig. 5 shows quartan paroxysms.

5. SEPTAN TYPE. *Illustrative Case.* Henry. Female, aged nineteen years. Typhoid three years ago, rheumatism in childhood, pneumonia a few months ago. Pregnant. Well-compensated mitral obstruction. Repeated examinations of blood for malarial parasite gave negative result. Rise of temperature accompanied on two occasions by chill, once by vomiting. "The inference that the fever is dependent on the heart lesion is based on the fact that no other cause could be found for it." Patient recovered.

This case is the only one of pure septan type that I have been able to find, though septan paroxysms have occasionally occurred toward the end of cases which at other times had followed other types. Fig. 6 shows the septan type.

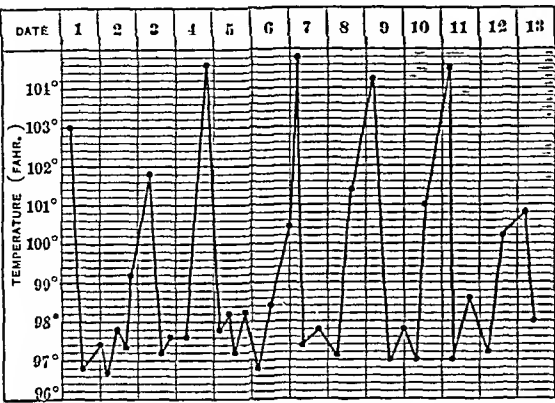
6. MIXED TYPES. These may be dismissed with a few words. The term is employed to designate only those cases which present two different types simultaneously. Such cases must be extremely rare. I have not been able to find even one which followed this course uninterruptedly. However, since Finlayson's case presented mixed tertian and quartan paroxysms during two months of its course, it seemed necessary to include the "mixed types." Fig. 7 is a part of the temperature chart of Finlayson's case.

7. IRREGULAR TYPES. The irregular types constitute by far the majority of cases of infective endocarditis which bear resemblance to malarial fever. The resemblance rather dates back to the time, however, when exact knowledge of the malarial parasite had not been acquired—when cases were diagnosticated as malarial fever simply because of recurring periods of pyrexia. No less an authority than Dreschfeld states, in Allbutt's *System of Medicine*, that all cases of chronic infective endocarditis resemble malarial fever. Such a statement is, to say the least, unfortunate.

The irregular acute cases are generally so clearly septic and the constitutional symptoms so marked that there is little difficulty in recognizing them, while the chronic cases are generally so irregular and so frequently develop in the course of chronic cardiac valvular disease that one is not left long in doubt as to their real nature.

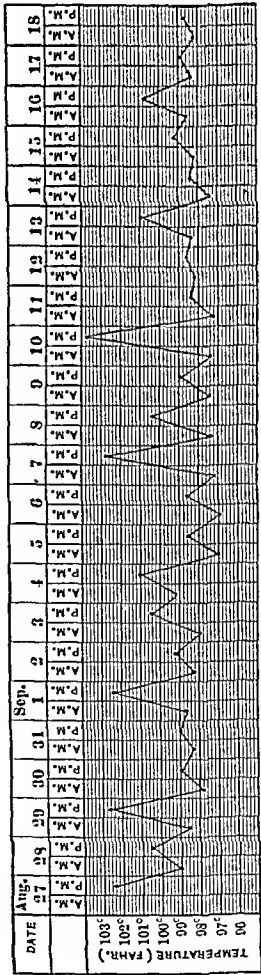
*Diagnosis.* The diagnosis of a pseudomalarial form of infective endocarditis is often very difficult. As in other varieties, the heart

FIG. 4.



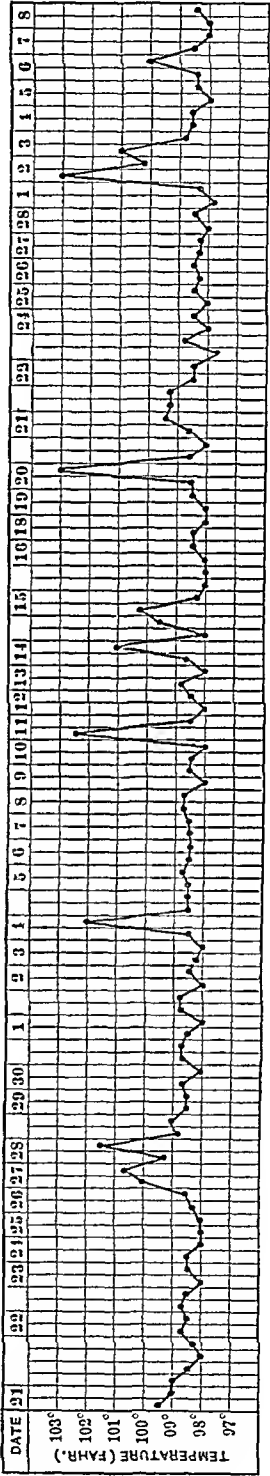
Tertian type. Portion of chart of Finlayson's case.

FIG. 5.



Quartan type. Wenckelbach's case.

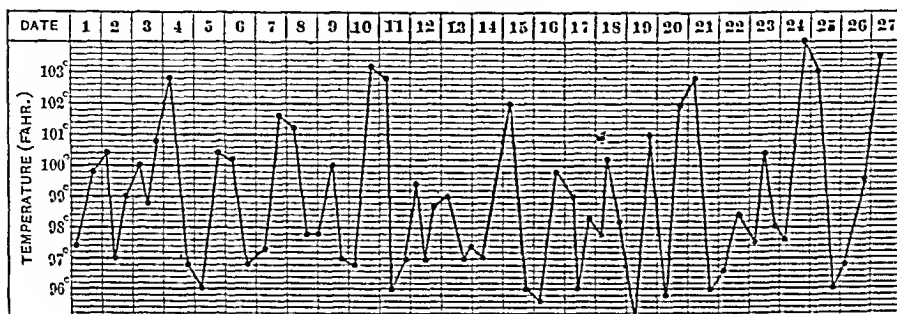
FIG. 6.



Septan type. Henry's case.

may give neither signs nor symptoms. If the infective process has been engrafted upon an old valvular lesion, the diagnosis need not present much difficulty, nor if an atrium of infection can be found. But the cryptogenic cases, occurring in persons previously healthy, or in those who, living in suspicious localities, give histories of recent apparently malarial attacks, may severely tax the skill of the clinician. As already mentioned, the disease is subject to sudden and

FIG. 7.



Mixed tertian and quartan types. Portion of chart of Finlayson's case.

complete, though temporary, interruptions. The patient may have been taking quinine. Under the circumstances, what is more natural than to assume that the quinine has stopped the paroxysms, even though the blood may not have shown the malarial organisms? When the patient returns for treatment, or if he comes with such a history, the existence of malarial infection is presumptive, and the case may go unrecognized, at least for a time. Then the failure of quinine to mitigate or arrest the paroxysms gives the first intimation that the patient is not suffering from malaria—assuming, of course, that a complete examination of the blood has not been made. Such an examination will at once rule out malaria, but, on the other hand, the presence of the malarial parasite does not necessarily exclude infective endocarditis (*vide* Herzog's case).

In infective endocarditis there is generally though not always leukocytosis; in malaria, leukopenia is the rule, except during a paroxysm. In infective endocarditis the polynuclear leukocytes are increased; in malaria there is relative lymphocytosis. Pigmented leukocytes are found in nearly all severe and protracted or fatal cases of malaria. The red cells and hæmoglobin show much the same changes in both conditions—rapid, marked oligocythæmia, hæmoglobin reduction, and degenerative changes in the cells. The changes are essentially those of secondary anæmia, though sometimes in malaria they pass into the pernicious type. The recovery of the infective agent from the blood is often possible and always conclusive, provided no other nidus than the heart valves can be found.

One of the remarkable features of these forms of infective endocarditis is the strength of the patient between the paroxysms. Until the disease is advanced he may feel quite well, and the classical picture of sepsis be lacking. Changes of type commonly occur during the course of the disease, and should be of much aid in diagnosis. In Ord's case, for example, the type changed from quotidian (two weeks) to tertian (two weeks), then to quartan, and later became irregular, the paroxysms recurring sometimes at intervals of a week. If an obstructive valvular lesion develops in a case pursuing a malarial course, the disease is almost certainly infective endocarditis. But, after all has been said, many cases will prove difficult to diagnosticate.

*Pathological Anatomy.* The simulation of malaria by infective endocarditis appears again in many cases in the pathological anatomy and histology of the viscera. In both diseases the long-continued hæmolysis results in the deposit of pigment in the spleen, liver, and bone-marrow, and while in malaria this pigmentation is much more extensive, owing to the activity of the parasites, nevertheless, the pigmentation of the viscera seen in septic processes often reaches a grade quite comparable to that of malaria. Thus, the spleen in septic processes may be considerably enlarged, distinctly brownish in color, and in very acute cases nearly diffuent. Likewise, the liver may exhibit a brownish or leaden color, much like that of malaria. Histologically, there is the same filling of endothelial cells of pulp and capillaries with masses of granular and globular pigment, the minute morphology of which is very similar in both malaria and infective endocarditis with bacteræmia. Hence it is unsafe to attempt to distinguish malaria from septic processes merely on the gross or microscopic appearance of pigment in the viscera. The only reliable method is the demonstration of the bodies of malarial parasites in cases of this disease, and their absence in septic processes. In nearly all other respects the pathological anatomy of pernicious malaria may be closely reproduced by septicæmia.

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## DISSEMINATED SYPHILITIC ENCEPHALITIS.

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THE following study is of a case of syphilis of the central nervous system, which presents points of interest in its pathological histology and as an example of the occurrence of severe syphilis of the nervous system soon after infection, at a time when the constitutional symptoms were still marked. There occur in the nervous system a variety of lesions, some of which may be regarded as specific; others cannot be differentiated from simple inflammatory phenomena. These inflammatory phenomena occur throughout the entire cortex, and also as focal areas of granulation tissue. These latter so overshadow the other features that it seems best to designate the case one of disseminated syphilitic encephalitis.

*Summary of the Clinical History.* C. C., male, aged forty-one years, admitted to the Danvers Insane Hospital, December 11, 1902. Family and early personal history not noteworthy. While not a steady drinker, he occasionally used alcohol to excess. June 12, 1902 he consulted a physician, giving a history of syphilitic infection three weeks previous, and then showed an initial lesion on the dorsum of the glans penis. On July 2, he was again seen by the same physician at a time when just recovering from an alcoholic debauch. The primary sore then showed extensive ulceration, and there was a papular eruption over the arms, chest, abdomen and legs. He was put upon a specific treatment of mercury, with occasional weeks of mixed treatment. An attack of iritis occurred, but soon disappeared with increased dosage. In the latter part of November, or about six months after infection, he had severe headaches which could be only partially controlled by treatment. Soon he became forgetful and was described as being "stupid." He was neglectful of his personal habits and "too stupid to eat." This condition led to his commitment to this hospital.

The examination made at his admission by Dr. Mitchell shows that he was poorly nourished, weighing 124 pounds. He was so

feeble that he was immediately put in bed. His face was dull and expressionless. He moved restlessly from side to side and made coarse purposeless movements with his arms. A general eruption was present; over the arms and legs this was of more or less discrete scaly papules, over the chest more of a maculopapular type. On the dorsum of the glans penis there was a recent scar. In the mouth were a number of mucous patches. The inguinal and epitrochlear glands were enlarged.

The left pupil was larger than the right. Light reactions could not be tested satisfactorily on account of the patient's restlessness. There was external strabismus of the right eye and partial ptosis of this lid. The knee-jerks were increased and there was a crossed adductor reflex. No ankle clonus. There was coarse tremor of the arms and hands. Tongue steady when protruded. Mentally, he showed extreme clouding of consciousness; only occasionally could his attention be gained and a relevant answer obtained to the question. Disorientation was complete. He was stuporous and frequently dozed during the examination.

*December 15th.* Stupor more marked; he showed coarse restlessness and moved purposelessly about the bed. He passed his urine and feces without control. His attention was obtained only by loud tones, and could not be held.

*17th.* Difficulty in swallowing, the food regurgitating through the nose. Ptosis of right lid more marked; slight external strabismus. Muscular twitchings of the right side.

*18th.* Comatose. Irritation of the left leg produced twitchings of the left leg and arm. Slight spasticity of right arm and leg. Left pupil larger than right; neither reacted to light stimuli. Died on this day.

*Autopsy Five and a Half Hours Post-mortem.* Male body, aged forty-one years, moderately well developed, but poorly nourished. Post-mortem rigidity is present only in the lower jaw. In the conjunctiva of the inner half of the left eyeball is a diffuse hemorrhage. Scattered over the thorax and abdomen are many yellow-brown scars; most of these measure a few millimetres in diameter, the largest rarely reaching 10 mm. On the arms are numerous papules with scaly tops. On the legs are many pigmented scars similar in appearance to those on the thorax; among these are scattered papules with scaly crusts; around the ankles are similar papules; the skin about these shows several small, scattered areas of ecchymoses.

*Heart.* Not notable save for a small hemorrhagic focus in the mitral valve.

*Lungs.* Considerable oedema and hypostasis in the posterior parts. In the left apex is a firm nodule 1 cm. in diameter.

*Microscopic Examination.* This nodule appears as a caseous substance surrounded by a thick fibrous capsule. Capillaries



throughout the section are intensely engorged. In some of the alveoli there are a few polynuclear leukocytes and epithelioid cells; many of these latter have inclusions of pigment granules; fewer have one or two red cells and occasionally a lymphocyte.

*Spleen and Kidneys.* Not notable.

*Liver.* Capsule of the left lobe shows a broad, milk-colored patch of thickening. Liver substance considerably engorged.

*Microscopic Examination.* Sections through the capsule show an increase of connective tissue with infiltration of lymphoid cells between the fibrils. The periportal connective tissue is much increased. Many of the central veins are engorged and the capillaries dilated. The liver cells of the central part of the alveoli frequently show fatty degeneration.

Sections through a papule of the skin of the arm show at one place an infiltration of the stratum corneum with polynuclear leukocytes, otherwise the epidermis is not notable. In the cutis there are places where accumulations of lymphoid and plasma cells and the fixed tissue cells are swollen. The bloodvessels here and in the subcutaneous areolar tissues have their walls crowded with plasma cells. The coil glands are strikingly free from cellular accumulations.

Sections through the glans penis show dense infiltration of the cutis with lymphoid and plasma cells among which are many mast cells. Focal accumulations of these cells lie deep in the tissue of the glans. The other internal organs show nothing unusual.

Cultures from the heart, spleen and meninges were negative.

*Head.* Calvarium and dura mater not notable. The pia mater of the convexity shows a slight haziness. Over the base, especially below the cisterna and from here spreading out over the pons and into the fissures of Sylvius on both sides, it is thickened, hazy, and hyperæmic. The thickening is most marked around the root of the right third nerve, and here the pia has a grayish, gelatinous appearance. The left middle cerebral artery, in the first part of its length, is considerably thickened.

The brain was sectioned after the method of Meynert, and in the gross showed nothing unusual except a small hemorrhage among the pyramidal fibres of the right side of the pons; here there is one hemorrhagic area about 7 mm. in diameter, around which are numerous small punctiform hemorrhages. The brain weighed 1360 grams. Save for a slight haziness of the pia, the cord showed nothing unusual in gross appearance.

At the autopsy some material for the following histological study was immediately fixed in Zenker's fluid and in alcohol. The remainder of the brain and cord were put into 10 per cent. formalin, and after a few days hardening the other material studied was cut and used for a variety of methods.

The descriptions of the meningitis are chiefly of material taken

from the frontal regions and from the pia at the base of the brain fixed in Zenker's fluid and stained with eosin and methylene blue.

That of the bloodvessels from similarly prepared sections.

The descriptions of cell changes of the cortex and cord are of alcohol-hardened material taken from the frontal, parietal and calcarine regions and various levels of the cord cut unimbedded and stained according to Nissl's method. Later further material was cut out from the formalin-hardened brain and put into alcohol and then stained in a similar way. The glia fibre studies are of material cut from the brain after a few days in 10 per cent. formalin and stained by Weigert's method; and of material cut the same as for Nissl's method but stained according to Benda's method for neuroglia fibres.

The medullated fibre descriptions are of material cut from the brain and cord after a few days hardening in 10 per cent. formalin and later put into Müller's fluid; afterward sections from these pieces were stained after the modification of Weigert's method described by Schaeffer.

*Meninges.* The characteristic lesion of the meninges—*i. e.*, the pia-arachnoid, is an infiltration of its meshes with cellular elements and proliferative and degenerative changes in its vessels, or a meningitis. The changes in the pia are so related with those of the vessels which lie in it that they will be considered together.

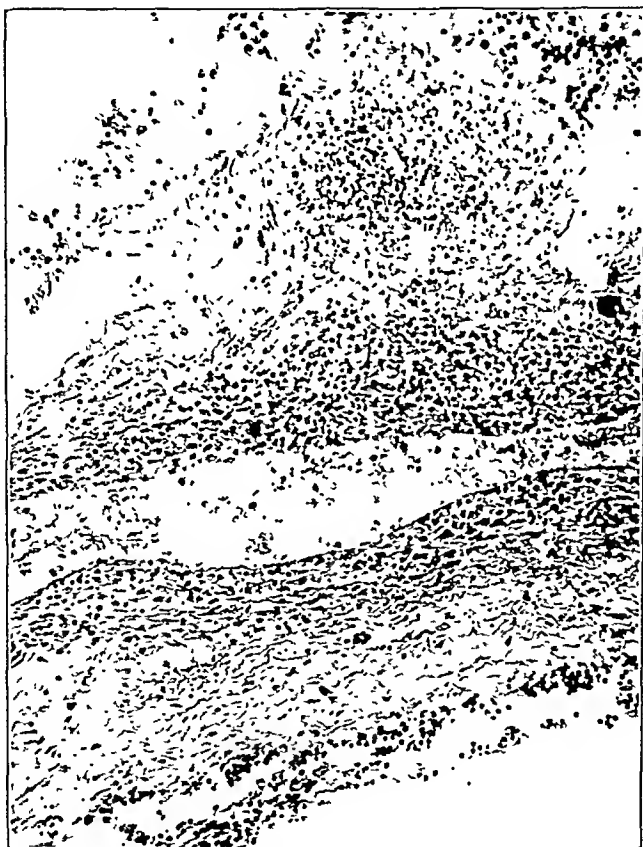
The meningitis shows local variations in its severity and in the character of its elements. In some places the pia appears quite normal; in others the meningitis is very intense. Generally the infiltration increases from a few cells lying in the deepest meshes of the pia to larger accumulations which distend the spaces and produce great thickening of the membrane. The greatest amount of infiltration occurs above and in the sulci. The exudate contains but little fibrin. The largest amount of fibrin, and this only a few threads, lies in an accumulation of polynuclear leukocytes in the region of a necrotic area. Where the exudate is least in quantity it is made up largely of lymphocytes arranged in a row compressed against the underlying cortex; among these are scattered a few plasma cells and occasionally an epithelioid cell, rarely a polynuclear leukocyte.

As the exudate increases in quantity the infiltrating elements spread into the upper meshes of the pia; epithelioid cells are here more common; plasma cells retain about the same relative proportion among the lymphocytes; polynuclear leukocytes are a little more frequently seen. In many places the exudate is so great that its cells lose all row-like arrangement and the meshes of the pia are torn apart; in these places the epithelioid cells not infrequently have inclusions of lymphocytes, usually one, but sometimes as many as six in a single cell.

There are places where focal accumulations of lymphocytes occur.

The exudate is always most abundant around the vessels and in these places shows the greatest variety among its elements. Plasma cells are always most numerous in the adventitia of the veins and here greatly outnumber the lymphocytes. Where the lymphocytes and plasma cells are intermingled, and in the exudate generally, it is possible to find, in sections stained by Unna's pyronin method, granules in the protoplasm of cells which in every other respect resemble lymphocytes; it is often quite difficult to distinguish between plasma cells and lymphocytes.

FIG. 1.



Vein in pia mater with necrotic nodule in the adventitia. Eosin-methylene-blue stain. Magnification 150.

The polynuclear leukocytes vary greatly in their distribution. Where the exudate is present in any considerable quantity they lie scattered at rare intervals. In some places they are in numbers and have a focal arrangement. This occurs in or near areas in which the tissues show necrosis, and is continuous with an infiltration of a vessel wall with leukocytes. There are a number of necrotic foci (Fig. 1); one appears as a knob-like mass projecting from the

adventitia of a vein. The media at this point is well stained but infiltrated with polynuclear leukocytes. The adventitia is in a characteristic necrotic state. The cytoplasm of its cellular elements stains poorly, and scattered everywhere through the area are nuclear fragments. Polynuclear leukocytes in various stages of disintegration are numerous. In these places there is a striking absence of lymphoid and epithelioid cells. With bacterial stains it was not possible to find any unquestionable micro-organisms. On the whole, apart from these focal areas where necrosis is present, the polynuclear leukocytes play little part in the meningeal exudate.

*Arteries.* The arteries of the pia show a variety of changes, the commonest of which is a proliferation of the connective-tissue cells of the intima; with this proliferation there is present an infiltration of the walls of the vessel.

In most instances the proliferation involves only part of the circumference of the intima. In a few arteries it extends completely around the lumen, but is then always of uneven thickness.

Not all of the vessels show changes, the majority appearing quite normal. The location of the arteries showing endarteritis seems to bear no relation to the intensity of the meningitis.

The endarteritis is not always present in those arteries around which the infiltration of the pia is most marked; and on the other hand, some arteries show severe endarteritis where the meningeal infiltration is very slight. The best general picture of the endarteritis is gained in preparations stained by Mallory's connective-tissue method. Normally the arteries of the pia, which are classed as of medium size, when stained by this method appear about as follows: bordering the lumen is a thin layer of blue fibrils, on which are red endothelial cells; this represents the intima, and follows the wavy outline of the underlying elastica, which appears as a homogeneous orange-red layer. Outside of the elastica is the media, with bluish fibrils interlacing among the red-colored muscle elements; external to this is the more or less broad layer of loosely arranged blue fibrils, or the adventitia.

The earliest changes in the endarteritis, in an artery of the same calibre, stained by the same method, are to be found in the inner blue layer, or the intima (Fig. 4). Where only a small segment of the circumference is involved in the proliferation, the remainder of the intima may not differ from the normal; but approaching the proliferated part, the endothelial cells of the intima together with a thin strip of the blue layer are loosened from the underlying homogeneous-appearing part which always remains in close contact with the elastica. The presence of epithelioid cells and an occasional lymphocyte beneath the loosened part seems to indicate that they have pushed the intima inward. Proliferation of the endothelial cells rapidly increases the thickness of the layer. Increasing number of epithelioid cells lie between the intima and the elastica

and push in among the proliferated fixed tissue cells. The cells of the intima at this point have the appearance of proliferating connective-tissue cells. They are spindle shaped, often branched, and the ends have a fringed appearance.

About these cells and interlacing among other elements of the proliferation are many blue-stained, connective-tissue fibrils. At the base of the intima there are other fibrils which are stained red or orange; for the most part these are coarser than the blue fibrils, but in a few places there are some that are more delicate and lie densely matted together. These latter red fibrils are probably fibrin.

The infiltrating elements beneath the intima and in the proliferation are for the greater part epithelioid cells; where the intimal proliferation is slight and the layer compact, a few lymphoid nuclei occur beneath the intima, but where the proliferated cells are loosely arranged there are many epithelioid cells. In a few instances quite large focal aggregations of epithelioid cells lie between the intima and the elastica.

One artery, the intima of which shows extreme thickening, has a row of peculiar homogeneous masses, extending at least a quarter around the circumference. They lie deep in the proliferation near the elastica. The elastica, however, is plainly visible beneath in an apparently unchanged condition. These masses appear as confluent plaques of no characteristic shape. They stain brilliant red by Mallory's connective-tissue method, and deep blue with Weigert's fibrin method; these are apparently a degenerative product possibly of the newly formed connective tissue. Unfortunately there are no preparations which could determine whether or not they are of hyaline nature. Smaller amounts of this substance are present in a few arteries showing large proliferations of the intima. Close to this red area is a large, round, finely granular mass which remains unstained in all of the methods used.

The elastica in all preparations shows only slight changes. In some of the preparations by Mallory's connective-tissue method it is more of a yellow than a red color, and opposite these places the intimal proliferation is most marked. In a few instances there is splitting off of a few lamellæ from the inner border of the elastica, but there are no infiltrating elements beneath these and it is probably due to some irregularity in the sectioning of the vessel.

The media is not often involved. In a few arteries it is infiltrated with lymphoid cells; this occasionally amounts to small focal aggregations. Rarely one sees long-drawn-out cells as if they were migrating through the wall. The adventitia is more frequently affected than the media but less than the intima. The process is an infiltration and not a proliferation. In one artery which shows no trace of endarteritis there are lymphoid and plasma cells scattered through the adventitia. Those arteries showing the most marked

proliferation of the intimal cells generally show the greatest adventitial infiltrations. One artery shows swelling of the nuclei of the adventitial cells; these are pale and have an invaginated margin; among them are scattered nuclei, which are much larger than the pale forms; often these have threads of chromatin grouped in their interior; one nucleus shows a mitotic figure. There are very striking differences between these two varieties of cells. Sometimes there is a band of lymphoid and plasma cells on the border between the media and adventitia.

FIG. 2.



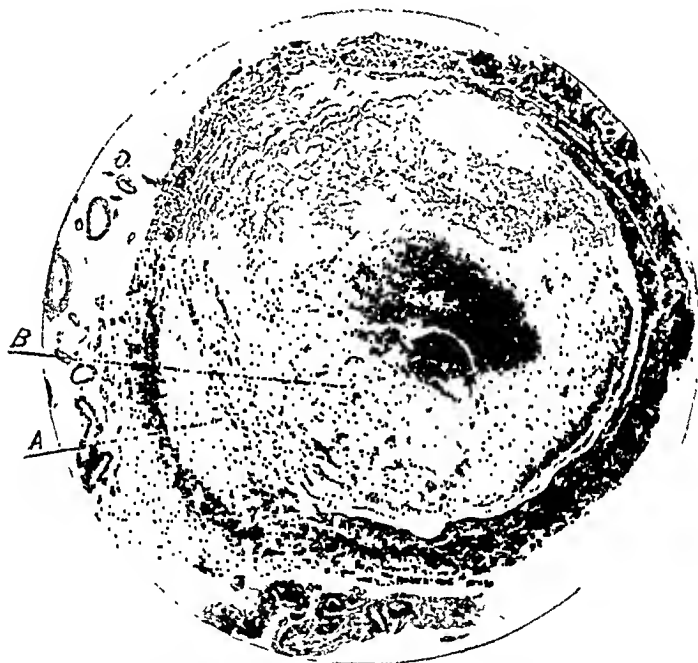
Vein in pia mater with swollen and infiltrated wall. Eosin-methylene-blue stain.  
Magnification 175.

A few of the larger arteries of the pia show at one point of their circumference a focal massing of polynuclear leukocytes, together with a few lymphoid and plasma cells. In most of these foci the form of the leukocytes is generally unchanged, but in some instances a focus is distinctly necrotic, the leukocytes staining poorly and their nuclei fragmented. In several arteries the necrotic focus is continuous with a similar focus in an adjacent vein. A number of these preparations were stained by methods for showing bacteria, and while in the débris there are scattered coccus-like particles, no significance can be ascribed to them, owing to the impossibility of here differentiating between organisms and nuclear fragments.

*Veins.* The veins of the meninges more generally show changes than the arteries. Commonly the larger veins are filled with red blood cells and relatively more polynuclear leukocytes than normal. In some there are threads of fibrin which in a few instances lie in

masses near the intima. The adventitia is usually infiltrated and its fixed tissue cells are swollen; these two processes give the vessel a somewhat increased size (Fig. 3). The infiltration, which is much greater than in the arteries, is made up of lymphoid and plasma cells, with a few epithelioid cells. In a few veins the walls are necrotic and at these places are densely infiltrated with polynuclear leukocytes; some of these latter contain inclusions of necrotic debris. The necrosis is more extensive than in the arteries and extends from the adventitia to the intima, but seems to be more advanced in the outer part of the wall, while next to the intima the leukocytes are best preserved.

FIG. 3.



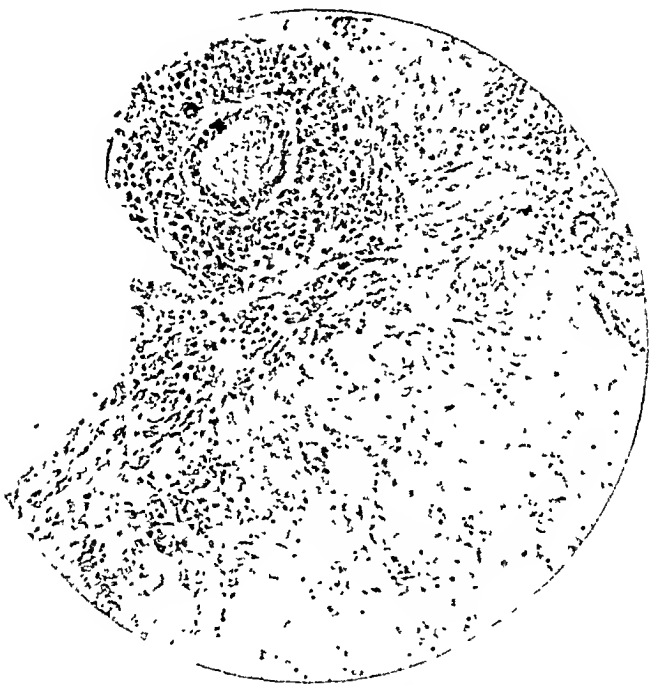
Middle cerebral artery. *A*, hemorrhage between media and adventitia. *B*, proliferated intima with adherent thrombus. Mallory connective-tissue stain. Magnification 30.

In the description of the meningeal exudate was noted the presence of a tumor-like mass, infiltrated with leukocytes, projecting from the adventitia of a vein (Fig. 1). The histological picture of this is not that of a gumma, but rather a focal massing of leukocytes at this point of the vessel wall, many of which have become necrotic.

In the gross examination of the brain, the left middle cerebral artery was thickened in its proximal part and was of a bluish-black color (Fig. 4). Sections across the artery at this point show great proliferation of the intima with a thrombus partially occluding its lumen. The proliferative changes in the intima are quite like those above described, excepting for some differences in the infiltrating elements; scattered among the proliferated intimal cells are many

polynuclear leukocytes and epithelioid cells. These latter usually have inclusions of yellow pigment; in some of these are red blood cells which still preserve their normal outline yet will not stain with eosin. The greater number of these phagocytes lie deep in the intima, near the elastica. Adherent to the proliferated intima is a thrombus composed for the larger part of a fine, granular-appearing substance which stains poorly; in this are many branched fibroblasts and a few epithelioid phagocytes. In cross section the thrombus fills a little more than one-fourth of the lumen; the remainder of the space is packed with red blood cells, among which

FIG. 4.



Hypertrophy and hyperplasia of glia cells in the superficial layer of the cortex. Adherent to the cortex is a piece of pia mater with a swollen and infiltrated vein. Nissl stain. Magnification 100

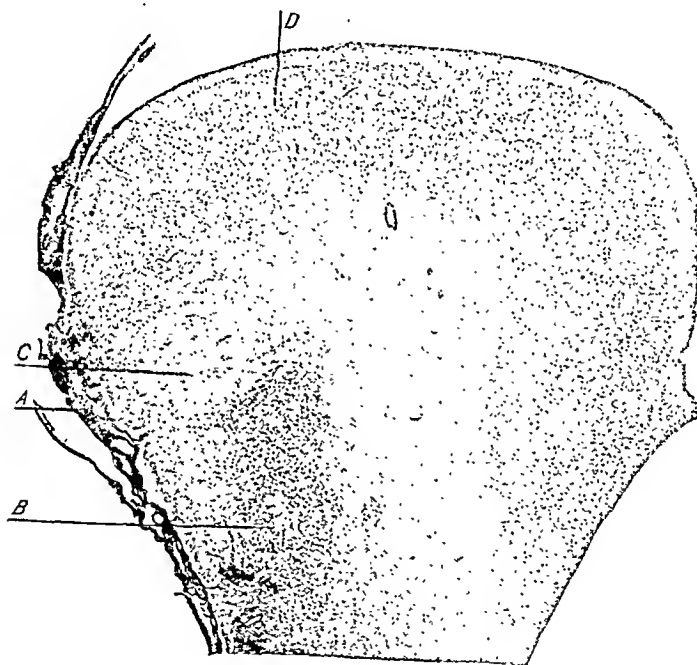
are fibroblasts and scattered small clumps of fibrin. There are a few epithelioid phagocytes with inclusions of yellow pigment or pale shadows of red blood cells. The media of this artery, excepting for a small segment, is of loose structure, and contains a number of infiltrating cells; some of these are long, compressed forms as if in process of emigration. The infiltration is very abundant at the point of attachment of the thrombus. At the point where the intimal proliferation is greatest there is a small hemorrhage between the media and adventitia, and both adventitia and media here show their greatest infiltrations; polynuclear leukocytes are quite numerous and often show necrosis.



It seems best to describe the changes in the brain substance according as they are diffuse or focal.

As diffuse changes in contradistinction to focal are included, those changes in the brain substance occurring apparently independent of foci of encephalitis or hemorrhages. It is not possible to place sharp distinctions between the two processes, as diffuse processes show greater intensity at some points than at others. The diffuse process is characterized by degenerative changes in the nerve cells, and by degenerative and proliferative changes in the glia and vessels. No section of the many examined is free from changes, although in the majority they are very slight.

FIG. 5.



Frontal convolution. *A*, pia mater. *B*, area of encephalitis. *C*, bordering zone in which nerve cells have been destroyed and where glia and non-nervous elements show proliferative changes. *D*, comparatively uninjured nerve-cell layers. Nissl stain. Magnification 10.

*Low Magnification.* In most sections there is present a hypertrophy and hyperplasia of the glia cells of the superficial layer of the cortex. The degree of this varies greatly, at some points being more marked than at others. The progressive changes in not a few places are so great that the contrast between superficial layer and nerve cell layers is obliterated (Fig. 3).

Sections from regions but slightly changed show no disturbance of the normal cortical architecture. In regions severely altered there are patches from which the nerve cells have disappeared, and those which remain appear shrunken and severely diseased (Fig. 5).

In these latter regions the substance between the nerve cells is strewn with disintegration products of nerve cells and obscured by the swelling of the glia cells.

*High Magnification.* Sections from the regions least altered show only slight disintegration of the Nissl bodies of the nerve cells. Many nerve cells are quite normal.

In the more severely altered regions, such as those showing under weak magnification evidences of nerve cell destruction and disappearance, there are present a variety of changes in the nerve cells. Two of these changes are so characteristic and occur so frequently that one seems justified in regarding them as of especial importance in the general process present in the brain.

Among the nerve cells of such a region there are numerous dark, shrunken, angular forms, the apical process and dendrites of which are traceable a considerable distance from the cell body; the axone is similarly stained. Internally these cells present a fine, crumbly structure; no distinct Nissl bodies are to be made out; many cells appear to be filled with a fine, pale dust; others may be described as finely vacuolated or honeycombed. In a few cells no trace of cell structure lies between the nucleus and the cell wall. The nucleus is generally pointed; although in some of the cells the nuclear membrane is fairly well outlined, in the majority the membrane cannot be differentiated from the deeply stained homogeneous nuclear ground substance. The nucleolus has a tendency to assume irregular shapes.

Scattered among the nerve cells of such a region are dark-blue, homogeneous nuclei, about which lie pale granules; these are evidently end stages of cells destroyed in the above type of alteration. This type of change rarely is distributed all through a region, occurring only where the cortical changes are most severe. Among or not far from such cells commonly occur others showing an entirely different type of alteration. Forms quite similar to this type occur among the nerve cells persisting in or bordering foci of encephalitis.

In the second type of alteration the nerve cells are swollen; the dendrites and axone are traceable far from the cell; within the cell the granules have disappeared, leaving the cell body filled with a pale meshwork; this latter is sometimes so faintly visible that the cell has almost a homogeneous appearance. The nucleus usually presents a pale-blue, homogeneous appearance and its membrane is invisible. In a few instances the nucleus is indistinctly mottled. Frequently two or more coarse granules, staining an intense blue color lie within the nucleus. In some cells the nucleus becomes irregular in outline, and as the granules within the cell disintegrate it fades away. The nucleolus takes on a mulberry-like form. Ultimately all traces of the cell structure disappear. Not infrequently these cells show deeply stained particles of substance lying

on or about the cell; sometimes these are massed at the base of the cell or at the tip of the axone. These are what Nissl regards as degenerations, and as incrustation upon the pericellular net.

This last type of alteration is not a common one. In no other cortex have we seen it in such numbers. It is a very severe condition and is always associated with various end changes of the same general type of alteration.

In addition to these two types of cell changes there are isolated examples of Nissl's "grave alteration," a type of alteration in which the body of the nerve cell breaks up into small characteristic ring-like degeneration products, the nucleus atrophies, and finally the entire cell disappears. There are a few cells which show the experimental axonal reaction; this is characterized by swelling of the cell with disintegration of the Nissl bodies, always more marked at one side of the cell. The nucleus, at the same time, takes a position close to the wall.

While the alterations among the nerve cells are varied and apparently all of a regressive character, the glia cells, excepting in a few places where the tissue injury is extreme, show progressive changes of a constant character.

There is a good deal of uncertainty as to just which of the nuclei present in the cortex are glia elements; there are, however, certain forms which are easily identified and which, in their progressive development, show constant characteristics in their transitions up to forms which are unquestionably glia cells.

The earliest stage in these progressive changes is swelling of the nucleus with an increase in size of its contained chromatin granules. At the same time there is noticed, spreading around the nucleus, a substance characteristic in its peculiar speckled or granular appearance. In the further development this substance becomes more compactly arranged about the nucleus and assumes the form of an oblong or oval cell body with radiating, process-like extensions; the nucleus takes an eccentric position, bulging from one side of the cell; gradually the granular appearance changes to one more homogeneous; from this stage the tendency is to shrink into what one regards as of the ordinary astrocyte type. This cell in some of its stages is probably the fibre-producing form. In satisfactory preparations there are increased numbers of glia fibres where these types occur, and it is often possible to demonstrate fibres still attached along the sides of the cell body or processes.

Progressive changes occur among some of the glia cells in the superficial layer of the cortex in every section examined. The intensity of these changes varies greatly; while generally the glia cells are rather evenly distributed through the superficial layer in any one section, there may be in the same section a focal increase of cells which sometimes fills the entire thickness of the layer (Fig. 3).  
the.

The glia cells of the superficial layer show more fully developed forms than those of the nerve cell layers, excepting where there are areas of severe tissue injury. The changes present in this layer appear to be intimately related to the changes in the pia mater. Where the meningitis is most intense there occurs the greatest reaction in the underlying glia cells, and where the meningitis is slight the glia reaction is not marked and is confined to the upper margin of the layer. Similarly, where there are areas of encephalitis lying in the more superficial part of the cortex there is always seen a marked glia hyperplasia.

In these areas of focal accumulations of glia cells, and where the glia cells have large cell bodies, it is always possible to demonstrate with elective staining methods that the glia fibres are also increased.

The glia cells of the nerve-cell layers show earlier and less intense changes than those of the superficial layer. No section is free from changes. In regions which show no foci of encephalitis the cell body is rarely completely developed, the cells showing the earlier progressive changes. Where the alterations in the nerve cells are slight, there occur swollen glia nuclei lying in a mass of delicately speckled protoplasm; sometimes these lie in groups of two or three. Where the nerve-cell changes are severe, and where the ground substance of the cortex is strewn with the débris of disintegrated nerve cells, the glia cells show the more advanced changes. There are a few places where the whole cortical structure shows severe injury, and in these there occur among glia cells showing progressive changes dark nuclei, which are apparently regressive forms of glia cells.

The distribution of the glia changes in the nerve-cell layers is peculiar. There is an unevenness in their distribution and a tendency toward focal variations in intensity. In a few areas where the nerve-cell changes are very severe, many cells having disappeared, the glia changes are very slight.

There occur in the cortex other forms of nuclei, the nature of which are not at all certain. One of these is a long, spindle-shaped cell, which Nissl calls a "Stäbchenzelle;" this is present in almost every region studied and appears as a long nucleus with coarse chromatin granules and filaments of cell-body substance projecting from either end. These cells will be described later.

Another form is the satellite nucleus; these are so few that they apparently play no part in the process present. There is one point which may be of interest, and one which is often illustrated in other processes, namely, that these satellite nuclei show no changes in regions where the glia nuclei show the most characteristic progressive alterations.

Other types of nuclei present in the nerve-cell layers are related to focal processes and will be described in that connection.

In general, it can be said that these changes in the glia cells are more delicate indications of the changes present in the cortex than

are the changes in the nerve cells. In some regions where it is not possible to regard the nerve cells as altered, the glia cells show distinct though very early changes.

The white substance of the cortex shows these diffuse changes to a far less extent than the nerve-cell layers. Those changes which one finds in the glia nuclei are apparently always of a focal character, dependent either upon vascular lesions in their neighborhood or they are reactions secondary to foci of encephalitis in the overlying nerve-cell layers.

**BLOODVESSELS.** In the regions showing more or less diffuse alterations, two apparently different changes are seen in the bloodvessels. These two types are: 1. Infiltration of the vessel walls and perivascular spaces. 2. Swelling of the vessel walls.

1. *Infiltrations.* The vessels which extend in from the pia frequently have an extension of the pial infiltration into their walls and perivascular spaces. The distribution of these infiltrated vessels is peculiar; they occur in regions showing only slight changes in the cortex and in the neighborhood of vessels showing no infiltrations whatever. Rarely do they extend deeper than the upper nerve-cell layers. They are most common in the superficial layer at the bottom of a sulcus.

The infiltration in and about a vessel wall is never very great. Generally there are only a few nuclei present. In this infiltration there occur lymphoid and plasma cells, epithelioid cells, with inclusions of pigment, and rarely a mast cell. These cells lie in the adventitia and perivascular space. Sometimes lymphoid cells alone are present, and sometimes only plasma cells, more generally the two occurring together.

Occasionally there are infiltrations of the walls of vessels lying deep in the nerve-cell layers and which show no connection with the pia, at least, not in the plane of the section studied; there is no uniformity in the distribution of these vessels.

In no way can it be seen that these infiltrations differ from those associated with general paralysis, either in the character of their constituents or in their localization in the vessel walls. In most cases of general paralysis, however, the infiltrations are larger, but there often are cases in which they are not more marked than here.

2. *Swelling of the Vessel Walls.* This is a change present in varying intensity in every region studied; it is always less marked where the changes in the nerve cells and glia are slight and is greatest where these are most severely altered. As this process is nowhere as marked as in the lesions of focal encephalitis, it will be better to describe it later on in that connection.

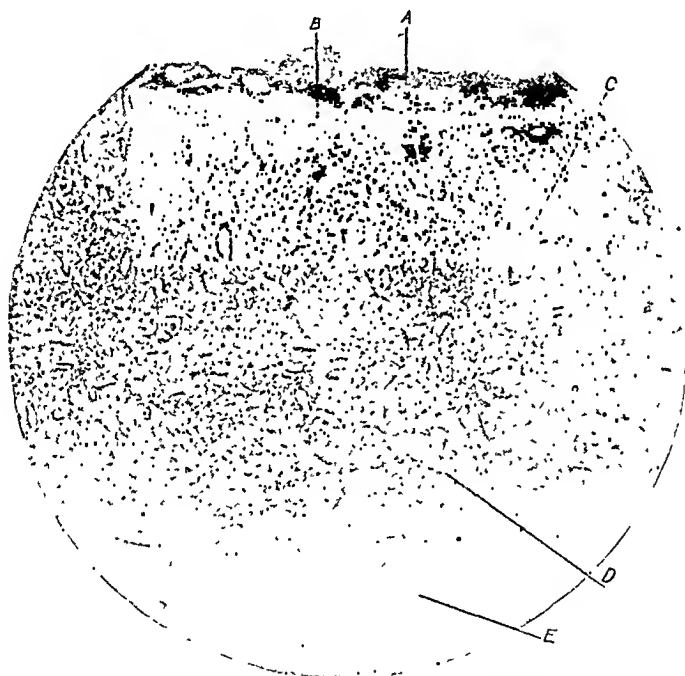
**FOCAL CHANGES.** As focal changes, there occur in the brain: 1. Areas filled with the elements characterizing granulation tissue or areas of encephalitis. 2. Changes of simple necrosis or softening, directly related to a vessel in their immediate vicinity. 3. Hemor-

rhages. 4. A few foci, which, from their compactness and similarity to the histological picture of a gummatous tumor, are so regarded.

In all of the focal processes it is necessary to discriminate between the primary process and various reactive changes in the elements bordering the focus. It is difficult to judge as to the relative or absolute number of these various focal processes. In the fresh brain it was not possible to identify the smaller foci, but after hardening in formalin many were picked out from their more or less marked contrast with the surrounding tissue.

As encephalitis we here describe a process characterized by death of the nervous elements proper, proliferative changes in the vessels,

FIG. 6.



Area of encephalitis. *A*, infiltrated pia mater. *B*, focus of granulation tissue. *C*, zones in which glia and non-nervous elements are proliferating. *D*, layer of epithelioid cells lying along the edge of (*E*) white substance. Nissl stain. Magnification 15.

and an infiltration of the area with epithelioid cells. Accompanying this process there are always reactive changes in the glia. The area is separated from regions in which the elements, while not normal, preserve much of their integrity by zones in which the elements show reactions differing according to their distance from the focal process.

It is not demonstrated that any of the foci are direct invasions of the process from the pia mater. In some instances, while the infiltration of the pia mater and that of the underlying cortical substance appear to merge into each other, on careful examination a difference between the two processes is seen. This is principally in the char-

acter of their elements. In the pia the predominating cell is the lymphocyte, while in the underlying cortex it is the epithelioid cell which occurs in greatest numbers, lymphocytes being quite rare. The upper part of the superficial layer of the cortex contains strikingly fewer cells than the regions on either side and forms a boundary zone between the dense infiltrations of epithelioid cells below and the meningeal exudate above.

FIG. 7.



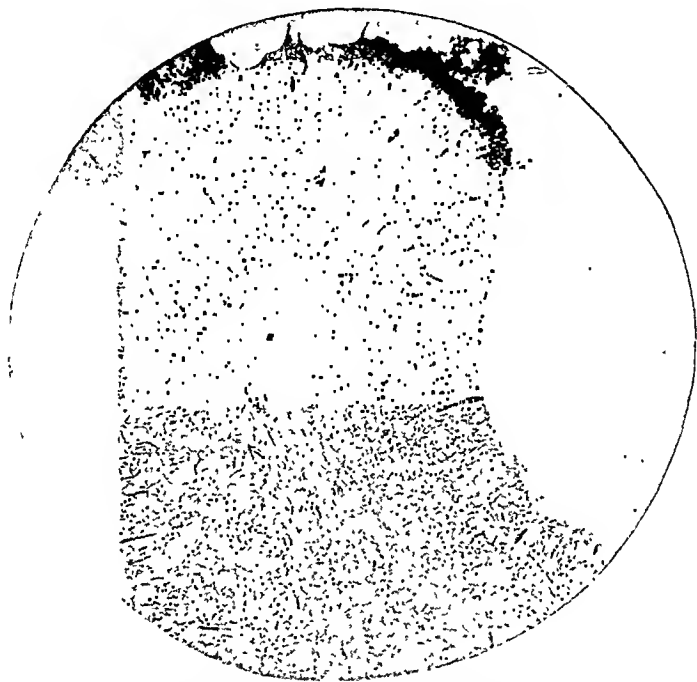
Epithelioid cells and swollen vessels from the outer edge of encephalitis area. Nissl stain.  
Magnification 225.

Each of the larger foci of encephalitis is limited primarily to the nerve-cell layers of the cortex. In some instances it involves all of the layers; in others its upper level reaches the position of the layer of small pyramidal cells. (Figs. 6, 7, 8.)

In the earlier stages of the process these areas of encephalitis are separated from the white substance by a border of closely packed epithelioid cells. Later this sharp demarcation is less prominent. The focus is bordered on either side by zones in which there is a

reaction differing in intensity according as they lie close to or removed from the focus. One of these foci, under low magnification, shows the normal cortical architecture entirely changed. Nerve cells are not to be distinguished, and the area is filled with swollen vessels and pale cellular elements (Fig. 7). Under the immersion objective not a normal nerve cell can be seen. Here and there lie dark cells, which, from their general appearance, seem to be the remnants of former nerve cells; such also are scattered, shadow-like pyramidal forms, which have a faint yellow tinge.

FIG. 8.



Frontal convolution, the entire area showing encephalitis with almost total destruction of nerve elements. Nissl stain. Magnification 15.

Most striking in one of these foci are the swollen bloodvessels and the large numbers of epithelioid cells crowding the area. All of the bloodvessels are swollen; as their individual cells increase in size and become broader, their protoplasm has a tendency to stain deeper. In some cells the protoplasm has a granular appearance and is usually more dense at one pole of the cell; this part of the cell stains an intense blue color in Nissl preparations. The nucleus increases in size; its interior has a glassy, homogeneous appearance and rarely is it possible to distinguish the chromatin network. The nucleolus is large and of a characteristic blue color; often its outline is oblong or otherwise irregular; occasionally there are from one to three small, deeply stained granules scattered around the nucleolus.

This swelling of the cells of the walls gives the vessel a laminated



appearance. It occasionally seems as if the vessel is a mere nest of concentrically arranged cells. The lumen is almost obliterated; sometimes a leukocyte or red-blood cell is pushed in among the cells of the walls. The normal compact structure has become loosened and the cells are pushed apart. Some vessels cut in their long direction seem as if their walls are split into two layers. A few of the cells show mitosis. The relation of these swollen cells of the vessel wall to the epithelioid cells abounding in their neighborhood is interesting. In the process of swelling some of the outer cells of the wall become loosened at one end; this end is often noticed projecting free from the wall. While the cells which belong positively to the vessel wall are compact and lack the spongy or vacuolated appearance of the free epithelioid cells, it is common observation that as soon as a cell shows indications of loosening from the wall of the vessel its protoplasm appears less compact. It seems quite possible to trace all stages between the swollen cells of the outer parts of the vessel wall and the epithelioid cells lying free in their neighborhood.

It is notable that the epithelioid cells are most numerous near those vessels which are most swollen; while around the vessels in the peripheral parts of an area of encephalitis they are not found in large numbers. Some of these swollen vessels, notably the larger, have lymphoid and plasma cells crowded in among the cells of their walls, and in places appear quite the same as the infiltrated vessels in other parts of the cortex where the tissue injury is less marked. From the study of this and similar foci, it seems as if the swelling of the walls and infiltration are two separate processes, the latter process being more chronic.

The epithelioid cells crowding the focus of encephalitis for the most part do not differ from those found in the areas of inflammation of other organs. They are the "Körnchenzellen" of German descriptions and correspond to the cells which abound in the early stages of anæmic softening of the brain. There are some cells present in considerable numbers which show a great variety of form; the body of these cells is sometimes long, with branching protrusions from one end, or a part of an irregular-shaped body may be extended like the pseudopod of an amœba. These cells are always coarsely vacuolated; in some there are yellow-tinged inclusions; many have large spaces, like digestion vacuoles. What these cells are is difficult to decide.

Another type of cell occurs in few numbers in the central part of the areas of encephalitis, but is very numerous in the bordering regions. About one of these foci it is distributed in ill-defined zones, in each of which it shows phases of development different according as they are near or far from the parts showing the more severe general tissue changes. In regions more or less removed from areas of encephalitis, where only slight general changes are noticed in the nerve cells and glia, there occur scattered in few numbers long pale

nuclei, with a rather indistinct, filament-like cell body extending from either end. These nuclei are oblong or fusiform; in Nissl preparations they stain more of a greenish color than the ordinary glia nuclei and contain a number of coarse chromatin granules. The cell-body substance is slight in amount and finely granular in structure. In this stage it corresponds evidently with what Nissl describes as the "Stäbchenzelle," a form occurring frequently in the cortex of general paralysis. Nearing the focus of encephalitis there is an increase in the number and size of these forms; they have become longer and broader; the cell body is coarsely meshed and vacuolated; along the edge of a focus of encephalitis there are branched forms, apparently of the same element; the cell wall is here sharper outlined; the nucleus appears to be placed nearer to one side, and the cell body becomes more loosely partitioned and seems to be in a process of channelling through. Often two or more will be joined at their ends or at the tip of a branch. In a few instances it seems as if they are directly connected with the wall of a delicate vessel. It is difficult to decide what the origin and function of this type of cell are. The cells differ in so many ways from glia elements that it seems certain that they are not of this class. They are also not of the type of the common epithelioid cell. There are evidences that they are related to the process of forming new vessels, but no positive conclusions can yet be stated. We have seen this form and the large branched vacuolated phagocyte cell in simple encephalitis after trauma, and the former is not uncommon in various organic brain diseases, notably general paralysis, where the formation of new vessels is often quite prominent.

Other cellular elements present in one of the foci of encephalitis are glia cells in various progressive stages. Most of these show hypertrophy of the cell and nucleus. The nucleus is large, containing coarse chromatin granules and lying at a corner or side of a more or less homogeneous cell body, from which project short, stubby processes. In these foci the glia cells are always fewer than in the bordering regions; in the older parts of the focus the glia cells are shrunken and present the form of the common astrocytes.

Scattered through the focus are various nuclei difficult to identify; some are like the lymphoid nuclei occurring elsewhere. Many are nuclei apparently regressively altered. In preparations by Nissl's method these appear as dark-green nuclei of irregular outline, and usually of a homogeneous structure; in some it is possible to distinguish a few dark granules. Polynuclear leukocytes are very rarely seen.

The areas of encephalitis are bordered by zones which show changes different from those present in the area itself, and are a combination of the changes which we have described as diffuse and those caused by reaction secondary to the encephalitis (Fig. 6, c).

Each focus is bordered by a zone in which nerve cells are few;

great numbers of them have disappeared, and those remaining are in various regressive changes leading to complete destruction of the cell.

The vessels are swollen and show proliferative changes, which are, however, never as prominent as in the focus itself. Many show the adventitial infiltrations seen all through the cortex. In this zone lie large numbers of the peculiar long cells described earlier. Epithelioid cells are few and lie close to the margin of the focus and always alongside of a vessel. Hypertrophied glia cells are numerous; these have swollen nuclei, always of a characteristic glassy appearance, and differing in this stage from all the other nuclei present; the nucleus contains one or more coarse lumps of chromatin; surrounding the nucleus is a protoplasmic body; in the greater number of cells in this zone this appears as a large, bulging, homogeneous mass with short, stubby processes. In the older of these the border seems to take a deeper stain than the rest of the body. This type represents the fully developed hypertrophied cell, and between this and the earlier progressive changes there are all stages. Some of these cells have two nuclei; none show mitosis. There are a few glia cells occurring in places where the tissue injury is most severe, which have swollen, loosely-meshed cell bodies, which stain poorly; occasionally there are the peculiar forms of glia which Nissl calls "Gliarosen." These are "mould-like" masses of spreading protoplasm, in which lie clusters of glia nuclei.

The white substance of those regions where the cortex shows focal encephalitis has hypertrophied glia cells close to the focus. Only one region, and this where several foci are in one section, shows diffuse changes throughout the white substance. In this region hypertrophied glia cells are scattered everywhere. There are also many of those shrunken, dark, homogeneous nuclei described earlier as occurring in the focus itself. Epithelioid cells occur in moderate numbers. Close to the focus there are swollen vessels and delicate, newly formed capillaries.

In general, the vessels of the white substance are less altered than those of the nerve-cell layers. Occasionally there are infiltrations of lymphoid and plasma cells in their walls.

2. Areas of anæmic necrosis due to vessel changes—*i. e.*, simple softening. Apart from the areas of encephalitis, there are several regions which show the characteristic process of softening; these lie always in the course of the vessel, visible in the plane of the section. They are only seen along the deep or medullary arteries. One such focus of softening borders an artery extending through the nerve-cell layers into the white substance; around the vessel the tissue is of loose structure and infiltrated with epithelioid phagocytes. Formalin-fixed preparations stained with Scharlach R. show that these cells are crowded full of fat or myelin granules. The glia bordering these areas of softening always shows progressive changes. In a

number of places away from the foci of tissue injury the epithelioid cells in the adventitia or perivascular infiltration contain granules giving the reaction of fat.

3. *Hemorrhages.* There are no focal hemorrhages in the cortex. In the left internal capsule and in the left thalamus there are small punctate hemorrhages. Among the pyramid fibres in the right side of the pons there are a number of larger hemorrhages. Several smaller hemorrhages are present in the medulla. The nuclei of the ninth and tenth nerves on both sides are infiltrated with blood. In all of these regions the bloodvessels are intensely engorged; some of these are ruptured and their neighborhood is infiltrated with blood cells. Around one of these hemorrhages in the medulla the tissue is porous, such as occurs in early softening, but there is no demonstrable reaction of the fixed tissue cells. Always near these areas there are many round-shaped or irregular-shaped myelin bodies; there are no epithelioid phagocytes. The red cells have their forms well preserved and stain deeply with eosin. These facts seem to show that the hemorrhages present are very recent.

4. *Foci Resembling Gummatus Tumors.* Excepting for the focus of necrosis noticed in the walls of some of the meningeal vessels, there is nothing resembling a gumma in the brain above the medulla.

In the medulla there are several foci which in their histological picture correspond to gummata and differ essentially from the other focal processes described. One of these is in the pia around the root of one cochlear nerve. Here there is a focal accumulation of densely packed epithelioid-like cells, with many polynuclear leukocytes in the central part. The area stained poorly; many of the cells show characteristic necrosis. The mass of cells spreads into the pia along the course of the nerve and many push in among the nerve fibres.

A section passing through the lower part of the olive shows five small focal cellular accumulations in the gray substance around the central canal. These are composed of closely packed cells, having pale nuclei with coarse chromatin granules. These nuclei are of a variety of shapes; some are oval, or flask-shaped, or sharply bent at their middle. Most of the nuclei are bordered by a broad rim of protoplasm. These cells differ from those of the infiltrations of the vessel walls of this region; these latter always resemble lymphoid and plasma cells, while those of these foci are of the type of epithelioid cells. It seems probable that these are specific gummatus tumors.

MEDULLA AND SPINAL CORD. The pia shows an infiltration differing only in intensity from that of the convexity of the brain. Vessel changes are, however, more general. The majority of vessels are engorged with blood. Many have perivascular infiltrations; many show proliferative changes in the intima and adventitia. One artery in the region of the medulla has endarteritis and occlusion of its lumen by a partially organized thrombus. A few vessels show areas of necrosis in the media and adventitia similar to those found in the

meninges of the brain. It is not demonstrable that the meningitis is more marked at any special level of the cord further than that where the nerve roots are most abundant and the pia of loosest texture, as in the lumbar and sacral levels, the meningitis is more prominent than in other regions.

The walls of the vessels in the medulla are more generally infiltrated than those of the brain. Not only the vessels extending in from the pia, but those lying deep in the more central parts show larger accumulations of lymphoid and questionable plasma cells in their walls and perivascular spaces. The focal hemorrhages occurring here have been noted. Along almost the entire length of the medulla and cord the glia cells of the margin are hypertrophied. At one point there is a triangular area of hypertrophied glia cells extending deep into the medulla. There are no signs of an inflammatory process in this area.

Satisfactory preparations of the cord by Nissl's method show remarkably well-preserved nerve cells. Besides the hypertrophy of the glia cells around the margin there is a slight degree of infiltration of cells from the pia around the arteries and posterior root fibres.

In a section through the cervical cord there are present two small foci in the gray commissure in which the glia cells are hypertrophied.

Many sections from the medulla and cord prepared by methods for demonstrating the myelin sheaths show no fibre degenerations. Marchi preparations show scattered, blackened fibres among others which appear normal. These latter findings are so uncertain that they are not regarded as important.

*Fibre Degenerations of the Cortex.* Preparations were studied from many different regions, but only one of those shows any coarse fibre degenerations. This was from the left gyrus rectus (Fig. 9).

Even without magnification, there is noticeable a striking paleness of part of the white substance. When more highly magnified, the degenerated part appears to involve about a third of the white substance.

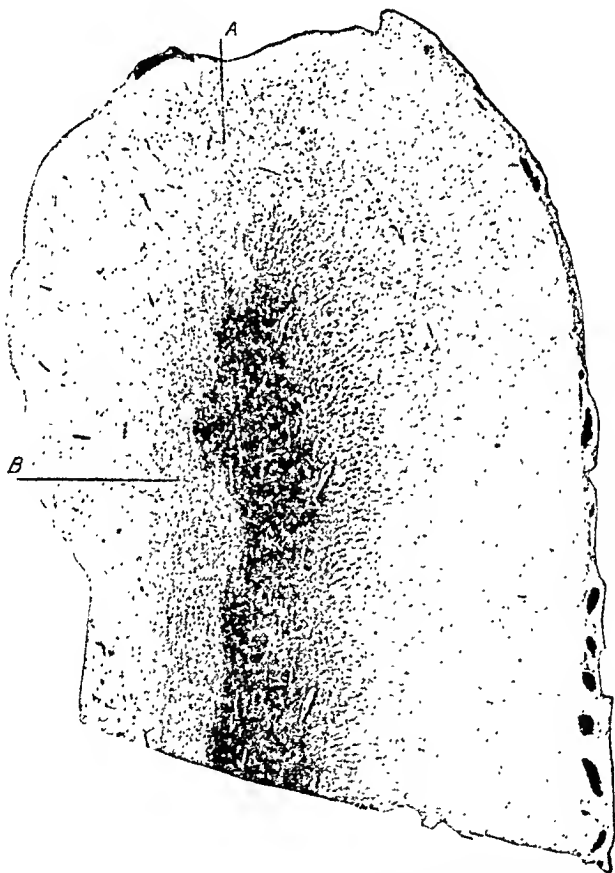
It is clearly demarcated from the normally stained part, but from this latter there passes into the degenerated part some fibres, either singly or in sprays, which are well preserved. The degenerated portion is made up of pale, barely visible fibres, among which are scattered a few that are well stained. It is easy to find evidences of degeneration among the fibres along the edge of the more normal part, principally flask-like bulgings of the fibres; these are also present in those stained which lie scattered through the degenerated area. In this section there are present in the nerve-cell layers two small and one larger area in which the nerve fibres are absent; each of these is bordered by fibres relatively as numerous as in other regions at this depth. Each of the areas show severe general tissue changes, and contain dark nuclei and an increased number of capillaries, which are much

engorged. In every way these agree with foci of encephalitis, as seen in more suitably prepared sections.

Above on either side of these areas there is a very distinct thinning of the tangential fibres. The larger of these foci lies directly above the part of the white substance from which the fibres have disappeared. Between the focus and the white substance only a few pale, radiating fibres remain.

While this is the only region which shows coarse changes, several others show finer degenerations.

FIG. 9.



Gyrus rectus. The fibres in the left half of the white substance degenerated. *A*, focus of encephalitis. *B*, area of fibre degeneration. Myelin sheath stain. Magnification 10.

In the right frontal convolution the tangential fibres of the superficial layer are in places reduced to a few isolated fibres, and at some points are entirely interrupted. In these defective places there is always noticed hypertrophy of the glia cells. The pia at this point also shows an intense infiltration. In this section, as in all of the others, it seems true that in this layer where the glia cells are hypertrophied the superficial tangential fibres are fewest.

In the left first frontal convolution there is a similar disappearance of the tangential fibres in the superficial layer. The same is true of the left and right anterior central convolutions. In the occipital regions no change is noticed in the fibres.

In analyzing the case the early occurrence of the disease of the nervous system is of clinical interest. In many of the text-books it is stated that syphilis of the nervous system is a phenomenon occurring late in the disease. There have, however, been a number of analyses of large series of cases, notably by Naunyn,<sup>1</sup> Gowers,<sup>2</sup> and Hjelman,<sup>3</sup> as well as a number of isolated cases, which show that syphilis of the nervous system often occurs within a few years or even within the first six months after infection (Oppenheim<sup>4</sup>). In our case the first nervous symptoms occurred within six months, and the entire course was completed in eight months after infection.

Anatomically, syphilitic disease of the central nervous system may manifest itself as: 1. Gummata. 2. Chronic hyperplastic inflammation. 3. Disease of the bloodvessels. To these may be added the parasyphilitic processes, such as those of tabes and general paralysis. It is not uncommon for all of these three to be present at the same time, and multiformity is quite characteristic of syphilis of the nervous system. This is notable in the present case.

In this case the most striking anatomical changes are those of the bloodvessels, while the production of focal gummata forms only a minor part of the process. In most of the reported cases of early syphilis of the nervous system lesions of the bloodvessels are more marked than focal gummata. Kahane<sup>5</sup> states that the diseases of the brain which occur in the early period of syphilis have the common anatomical character of almost always involving the bloodvessels, while gummata in the central nervous system, as well as in other organs, tend to occur late in the disease.

The meningitis present is a diffuse process and shows only a few questionable characteristics which would entitle it to be classed as a gummatus meningitis, the form which syphilis of the pia mater usually takes.

In its distribution and in the character of its elements it shows nothing specific. The great predominance of lymphoid and plasma cells and the rarity of polynuclear leukocytes give it the character of a chronic inflammation. These same elements are those which make up the meningeal exudate in general paralysis. It seems probable that the lymphoid and plasma cells appear first in the meningeal exudate, and that the occurrence of epithelioid cells and the few polynuclear leukocytes are related to differences in the severity of the tissue injury or of focal lesions of the coats of the bloodvessels. These latter cells are always found near vessels or where the exudate is in such quantity and the fixed tissue elements injured to such a degree that it is impossible to judge as to the source and the relation of the various cells to the primary process.

So far as can be determined, the cellular elements of the exudate differ little from those occurring in tuberculosis of the meninges; they, however, differ essentially from those of the acute infectious meningitides.

The intergrading forms of lymphocytes and plasma cells are interesting as showing the apparent close relationship of these elements.

Lesions of the bloodvessels are the commonest constant finding in syphilis of the central nervous system. According to Nonne,<sup>6</sup> they are seldom absent. Of the lesions, the endarteritis is the most familiar. In this case it is possible to study the process in an early stage. The first demonstrable step in the endarteritis is the lifting of the intimal endothelium by cells which pass in between the intima and elastica; the intima proliferation is secondary. Where these infiltrating elements came from was not determined. It is probable that they have wandered in from the adventitia, which in almost every instance shows local inflammatory changes. It is striking, however, how little the media is involved, as only rarely is it infiltrated, or can cells be seen which are in process of migration. The necrotic changes are always in the outer wall and spread from there inward. This necrosis is not unlikely the result of changes in the nutrient vessels of the adventitia. These findings accord with the position of Köster,<sup>7</sup> Friedländer,<sup>8</sup> and perhaps the majority of investigators, who regard the process as one spreading from the nutrient vessels toward the intima and do not regard the process as specific for syphilis; on the other side, Heubner<sup>9</sup> described the proliferation of the intima as the primary change due to direct action of the infectious agent of syphilis, the changes in the outer walls being secondary.

The thrombosis of the middle cerebral artery is apparently very recent. The intimal proliferation is not seen in the veins, but commonly there is present a mesophlebitis or periphlebitis. In the veins it is certainly noticed that the inflammatory process spreads from without toward the inner coat.

The pathological process in the brain and cord is characterized by multiformity. In the brain there is present a diffuse degenerative process affecting the nerve elements, glia and bloodvessels throughout the whole cortex. Apart from this, there are disseminated areas of encephalitis; these latter are apparently not dependent upon changes in the meninges. They show the phenomena of early granulation tissue, as well as local degenerative changes in the nervous elements and secondary reactive changes in the glia.

The hemorrhages, focal softenings, and the questionable gummata present are processes independent of these areas.

In its entirety the process may be classed among the few described cases of disseminated syphilitic encephalitis, as the inflammatory nature of the process seems to be the most prominent feature.

The frequent involvement of the meninges with lesions of the brain tissue has given the name meningo-encephalitis to a variety of



syphilitic processes of the central nervous tissue. In the strictest use of the term, it has been applied to those processes where the inflammation spreads into the brain tissue along the bloodvessels from the meninges. In some instances it has been given to cases where there was present a meningitis with a gliosis of the underlying adjacent brain tissue; in others where a meningitis was associated coincidentally with a process of simple softening. Apart from these, there are a few cases in which, in addition to a meningitis, there is present an independent inflammatory process in the brain tissue.

There is a good deal of confusion in the conception of encephalitis, and it is difficult to interpret many descriptions in the literature. This is true not only of syphilis, but of other brain diseases. The term encephalitis has been commonly applied to lesions which are those of an anæmic necrosis or simple softening. In other instances the description is that of a gliosis rather than an inflammatory process.

One is justified in regarding the process as one of syphilitic encephalitis where there occurs in syphilitic brain disease inflammatory phenomena in the brain substance independent of gummata, and not secondary to hemorrhages or the necrosis due to vascular obstruction.

Heubner,<sup>10</sup> in 1876, found, among some 150 cases of syphilis of the nervous system, 36 cases in which the process was regarded as one of simple inflammation. A careful analysis of 22 of the best of these descriptions convinced him that there was not a single case up to that time which could be regarded as a simple inflammation independent of a new-growth. In none of these cases was the histological examination thorough. In a few cases the inflammation might be ascribed to softenings in the neighborhood of a focal gumma overlooked during the examination. In many the inflammation was associated with meningitis. The remaining must be described as due to vessel disease, not focal.

It has not been possible to review all of the cases described as syphilitic encephalitis since Heubner's work. Many of the descriptions of the histological findings are incomplete, or no distinction has been made between the process of softening and that of an independent encephalitis. In others the phenomena of focal encephalitis are either described as extensions from the meninges or differ in essential ways from the case we have described.

A classical case often quoted in the literature is that of Charcot and Gombault,<sup>11</sup> in which there was present, in addition to focal gummata, independent areas of chronic inflammation. In the monographs of Bechterew<sup>12</sup> there are descriptions of a few cases which are regarded as encephalitis, independent of meningitis.

The best of these descriptions are cases of Oppenheim, Jürgens,<sup>13</sup> and Bechterew. In Oppenheim's case there was a focus of inflammation about 1 cm. in diameter in the pons and posterior corpora

quadrigemina; the brain arteries were normal, and he designates the case as one of encephalitis.

Jürgens has described a case in which at death there were signs of secondary encephalitis. At the autopsy there was found an acute universal encephalitis. He regarded the disease as exceedingly rare.

The most complete description we have found is a case of Bechterew's.<sup>12</sup> This case in its histology resembles our own case very closely. The course was somewhat longer. The first symptoms developed in the year following infection, and death occurred two years later. He names the case one of disseminated syphilitic focal sclerosis, and adds that it is the only case of this type which has been completely studied, both clinically and pathologically.

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## SOME OBSERVATIONS ON THE EFFECT OF ALTERNATING CURRENTS OF MODERATE FREQUENCY ON DOGS.

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THE extensive and accurate researches of Prevost and Battelli<sup>1</sup> leave little to be investigated as to the effects which follow, and the cause of death from the application of commercial electrical currents to animals. We think it desirable, however, that we place on record

<sup>1</sup> Journal de physiologie et de pathologie générale (1) 1899, tome i. p. 399; (2) p. 427; (3) p. 689 (4) 1900, tome ii. p. 755; (5) 1901, tome iii. p. 1085; (6) p. 1144.

some observations which we have had the opportunity of making on the effect of alternating currents of high frequency on anæsthetized dogs; the more so, since we believe that the observations throw some light on the cause of the variable lethal effect of such currents.<sup>1</sup>

Previous to Prevost and Battelli's papers considerable confusion existed as to the exact cause of death from electrical currents. d'Arsonval<sup>2</sup> and Kratter<sup>3</sup> ascribed death to respiratory cessation from paralysis of the bulbal centre; whereas, Tatum<sup>4</sup> and Biraud,<sup>5</sup> thought it to be due to arrest of the heart. Oliver and Bolam<sup>6</sup> came to the conclusion that currents of 200 volts act directly on the heart (*i. e.*, not through the vagal mechanism), but do not affect the respirations; with stronger currents, on the other hand, the heart and respiratory centre are simultaneously affected. Most of these workers further observed that the effect of the current and its lethality varies considerably for different groups of animals. Cunningham<sup>7</sup> concluded that fibrillary contraction of the heart was the usual cause of death.

Prevost and Battelli found that alternating currents of low tension (about 130 volts) cause only temporary arrest of respiration, but that fibrillary contraction of the ventricle is induced exactly similar to that which follows the application of a faradic current directly to the heart. In dogs these fibrillations always persist after the current is broken, so that, once the fibrillations have appeared, it is impossible to resuscitate the animal. In guinea-pigs and rabbits the fibrillations may sometimes disappear and the animal recover; whereas, in rats this latter result was invariably noted, this animal being apparently absolutely immune to low-tension currents. With very high-tension currents (1300 to 4800 volts), Prevost and Battelli<sup>8</sup> found that fibrillation of the ventricle does not occur, but rather that the beats become quicker and stronger, and that the arterial blood pressure rises. The respiratory centre, however, becomes paralyzed, and profound shock results. This respiratory paralysis could frequently be recovered from by the application of artificial respiration; and in dogs spontaneous reappearance of respiration was quite common. It was further noted that when the heart had come to a standstill—coincidentally with respiratory cessation—massage of it brought on fibrillation. Still another most interesting observation deserves notice, namely, that the application of a high-tension current to a heart already in fibrillary contraction causes

<sup>1</sup> These observations were concluded a year ago, but the publication was withheld in the hope of our being able to prosecute the investigation farther. This we find now to be impossible.

<sup>2</sup> Prevost and Battelli. *Loc. cit.*, No. 1.

<sup>3</sup> *Der Tod durch Electricität*, Leipzig, 1896.

<sup>4</sup> *Death from Electrical Currents*, New York Medical Journal, 1890, vol. lv.

<sup>5</sup> Prevost and Battelli. *Loc. cit.*, No. 1.

<sup>6</sup> *On the Cause of Death by Electric Shock*, British Medical Journal, 1898, p. 132.

<sup>7</sup> *A Text-book of Legal Medicine and Toxicology*, Philadelphia, 1903, p. 261.

<sup>8</sup> *Loc. cit.*, No. 2.

the fibrillations to disappear and the normal heart-beat to be re-established.

The other papers of Provost and Battelli refer to continuous currents (No. 3) and to the influence of the number of periods of the alternating current on its physiological effect.<sup>1</sup> In this latter research it was found that with very frequent alternating currents—*e. g.*, 1720 periods per second, a much higher voltage is necessary to produce death than when currents of low frequency (*e. g.*, from 9 to 150 periods) are used. It is also pointed out in this paper that the respirations, suspended during the application of the current, spontaneously reappear when the current is broken, provided the heart be not paralyzed. The other papers published in 1899<sup>2</sup> refer to the physiological effect of electrical discharges from condensers. Since these papers, others have appeared by Arloing,<sup>3</sup> Bordier et Lecomte,<sup>4</sup> and Guilnard,<sup>5</sup> but as there is nothing in any of these regarding the effect of alternating currents on dogs, a further reference to them will be unnecessary here.

Practically all the experiments carried out by us were with alternating currents, as used for illuminating purposes. In strength these varied between 400 and 2700 volts; in frequency sixty periods per second. In all cases dogs, rendered anæsthetic by morphine and A. C. E. mixture, were employed. The electrodes were made of copper or zinc, shaped either as thick rods, which could be placed in the rectum and mouth, or spoon-shaped, to apply to the surface of the body. The electrodes were usually wrapped around with a sponge soaked in saline solution, so as to increase the conductivity. The carotid blood pressure was recorded in most cases, and the respirations carefully observed.

The results of the experiments are summarized in the appended tables:

<sup>1</sup> Prevost and Battelli. *Loc. cit.*, No. 4.

<sup>2</sup> *Loc. cit.*, Nos. 5 and 6.

<sup>3</sup> Contribution à la connaissance de l'action des courants électriques continus à haut voltage sur les chevaux, *Journ. de physiol. et de path. génér.*, 1902, tome iv. p. 976.

<sup>4</sup> Effets de l'application directe des courants de haut fréquence sur les animaux, *ibid.*, 1903, tome v. p. 564.

<sup>5</sup> Contribution à l'étude des effets mortels produits par les courants électriques, *ibid.*, p. 363.

No.	Strength of current (volts).	Position of electrodes.	Duration of application.	Behavior (general) of heart and blood-pressure.	Behavior of respirations.	Lethal effect.	Remarks.
1	2300	Mouth and rectum.	5 sec.	Fall to abscissa.	Cessation.	Death.	Artificial respiration and massage of heart without effect; adrenalin intravenously.
2	1000	"	17 "	"	"	"	Artificial respiration and massage of heart without effect; adrenalin intravenously.
3	2300	"	Instantaneous.	Momentary inhibition.	Unaffected.	Recovered.	Same dog used as in 3a.
3a	2300	"	"	Fall to abscissa.	Cessation.	Death.	Artificial respiration and massage of no avail; adrenalin intravenously.
4	2300	"	15 sec.	"	"	"	1 mg. atropin sulphate injected previous to application of current.
5	2300	Back of head and hind limb.	Instantaneous.	Momentary inhibition.	Unaffected.	Recovered.	Same dog used in 5a to 5d.
5a	2300	"	"	Marked rise.	"	"	1 mg. atropin sulphate injected previous to application of current
5b	2300	"	1 sec.	"	"	"	
5c	2300	"	5 "	"	"	"	
5d	2300	"	20 "	Fall to abscissa.	Cessation.	Death.	
6	2300	"	Instantaneous.	Momentary inhibition.	Unaffected.	Recovered.	Same dog used in 6a to 6c.
6a	2300	"	4 sec.	Momentary inhibition, then rise.	"	"	
6b	2300	"	5 "	Momentary inhibition, then irregular heart action; became regular on massaging.	Cessation, but recovered by artificial respiration.	"	Artificial respiration and heart massage resulted in recovery of normal heart-beat and respirations; this is the only result of this nature that was obtained.
6c	4000	"	5 "	Fall to abscissa.	Cessation.	Death.	The resistance of the dog had been depressed by previous applications.
7	2300	"	2 "	Inhibition, then rapid beat.	Cessation, then recovery.	Recovered.	
7a	2300	"	10 "	Temporary inhibition.	Cessation, then recovery.	"	1 mg. atropin sulphate given previous to application of current.
7b	2300	"	10 "	Fall to abscissa.	Cessation.	Death.	Tissues at point of application of electrodes burnt; heat rigor of abdominal muscles.
8	2300	"	3½"	Fall to abscissa.	"	"	1 mg. atropin intravenously before electrocution; artificial respiration, heart massage and adrenalin injection without effect; P. M., auricles beating, ventricles in diastole.
9	2300	Leg and mouth.	2 "	Fall to abscissa.	"	"	Same measures as in 8 adopted without effect.
10	2300	Not recorded.	3 "	No effect.	Unaffected.	Recovered.	5 mg. atropin intravenously before electrocution.
11	2300	Head and leg.	Instantaneous.	Momentary fall.	"	"	Both vagi cut.
11a	2300	"	4 sec.	Fall to abscissa.	Cessation.	Death.	3 mg. atropin injection four minutes before application of current. 2.5 amperes passed through body; artificial respiration, adrenalin injection, etc., without effect.

No.	Strength of current (volts).	Position of electrodes.	Duration of application.	Behavior (general) of heart and blood-pressure.	Behavior of respirations.	Lethal effect.	Remarks.
13	1500 1 ampere	Head and leg.	2 sec.	Fall to abscissa.	.....	Partial recovery.	Artificial respiration and heart massage caused partial recovery of heart-beat and respirations, and dog came partially out of anæsthetic; readministration of anæsthetic (ether) caused death.
14	400	Head and foot.	Instantaneous.	Momentary inhibition.	Temporary cessation.	Recovered.	5 mg. atropin injected after application of current.
14a	600	"	"	Fall to abscissa.	Cessation.	Death.	Marked fibrillary contraction of heart.
15	800	"	"	Momentary inhibition.	.....	Recovered.	6 mg. atropin injected previous to application of current.
15a	800	"	"	Momentary inhibition.	.....	"	
15b	2300	"	"	Fall to abscissa.	Cessation.	Death.	Heart in marked fibrillary contraction; direct massage increased this
16	1000	"	"	.....	.....	Recovered.	No tracing taken; dog allowed to recover from anæsthetic; was in every way normal next day.
17	600	"	"	.....	.....	Death.	Marked fibrillary contraction.
18	400	On isolated heart.	.....	Fibrillation	.....	.....	Heart perfused by Langendorff's method (see text, p. 422).
19	400	On heart in situ.	6 sec.	Fibrillation	.....	.....	Perfusion of heart after fibrillations had appeared of no effect (see text, p. 422).
20	2700	Hind leg and head.	4½ "	Inhibition.	Cessation.	Death.	Window in thorax; heart quickly excised and perfused by Langendorff's method; auricles began to beat and ventricles to show fibrillations with occasional beats.
21	1500	.....	Instantaneous.	No effect.	No effect.	.....	
22	1000	Head and leg.	"	Momentary inhibition.	.....	Recovered.	Window in thorax.
22a	1000	"	"	Inhibition, then fibrillation.	.....	Death.	
23	1000	"	"	Inhibition, then fibrillation.	.....	"	Massage of heart; perfusion through coronary arteries with oxygenated Locke's fluid, anelectrotonus had no effect on fibrillary contractions.

The most noteworthy points of interest are: Firstly, the variable strength of current necessary to cause death; and secondly, the effect of the current on the circulatory system. By the study of the latter a satisfactory explanation is, we think, obtained of the cause of death in all cases.

With regard to the strength of current necessary to cause death, it will be noticed that this depends largely on the position of the electrodes. With these in the mouth and rectum death occurred

after a momentary application of 1000 volts (No. 2<sup>1</sup>); whereas, when they were placed on the head and hind leg a current of 2300 volts, repeatedly applied for periods of from one to ten seconds, did not cause death (Nos. 5, 6, 7, and 10). Even when the currents were similarly applied (viz., to back of head and hind leg), however, currents of equal voltage had a variable lethal effect; thus, in several cases 2300 volts momentarily applied caused death (Nos. 9 and 15), and this was also induced in some by a much smaller voltage (Nos. 14 and 17). After we have considered the effect produced on the blood pressure, we will be in a position to offer a satisfactory explanation of this irregularity in lethal effect.

The effect on the blood pressure is very striking; at first there is often a slight rise, then a distinct fall to below the abscissa, and then, if the current be only of short duration, a rise again to above normal. If the current be of longer application, however, the blood pressure does not recover. The temporary rise at the moment of application is probably due to muscular contraction and perhaps vasoconstriction. The inhibition which follows is due, in some cases at least, to stimulation of the vagus mechanism, for it could be prevented in one case by the administration of atropin (No. 5). Even when atrophinized, however, or when both vagi were cut (No. 11), this inhibition, with subsequent recovery, was not infrequently noticed, and in all cases where a strong current was applied for long enough (five to ten seconds), permanent fall of the blood pressure was observed, even when the animal was deeply atropinized. Obviously, then, vagal inhibition of the heart has nothing to do with the permanent fall of the blood pressure. By a direct examination of the heart, the cause of this permanent fall of blood pressure was found to be fibrillary contraction of the ventricle, the auricles, meanwhile, continuing to beat normally (Nos. 8, 11, 14, 15, 18, 19, 20). By directly applying the electrodes to the heart, the mode of onset of this condition was more closely studied. It was found that when the current was closed, there was entire inhibition of the ventricle, and that when the current was broken the fibrillary twitchings started at the base. A current of one volt directly applied to the heart was sufficient to induce the fibrillation.

In one experiment we excised the heart and perfused it through the coronary arteries with defibrinated blood by Langendorff's method. When the beats had become normal a momentary current of 400 volts was applied to the base. The normal beat was immediately replaced by fibrillary twitchings, which persisted until the heart was quite dead.

In another experiment, after producing fibrillary twitchings with the heart *in situ*, it was quickly excised and perfused by Langendorff's method; in about two minutes normal contractions of the

<sup>1</sup> These numbers refer to the table.

ventricles reappeared at the rate of 90 beats per second, but the fibrillary twitchings still persited.

Direct massage of the heart *in situ* was also frequently attempted, but without avail. Anelectrotonus, produced by using various strengths of voltaic current, was likewise without effect on the condition.

We had not an opportunity of applying a very powerful and rapid alternating current, which is stated by Prevost and Battelli (*loc. cit.*, No. 2) to arrest the fibrillation, nor did we cool the ventricle as practised by Porter<sup>1</sup> to dissipate the fibrillations produced by ligature of the coronary arteries. With the strongest current at our disposal (*viz.*, 2700 volts, No. 20), applied for 4.5 seconds through electrodes placed on the head and hind limb, we noticed that the heart was merely inhibited, fibrillation not appearing until after the heart had been excised and massaged by hand, in point of time, eleven minutes after the current had been applied.

The respiratory movements were invariably brought to a standstill during the application of the current, on account of the tonic convulsions coincidently induced. They reappeared, however, when the current was broken, provided this was only of so short duration that no fibrillary contraction of the heart existed. Whenever fibrillary twitching had occurred, however, the respirations remained permanently inhibited, and this was true, even after vigorous artificial respiration.

The application of a current of 1000 volts for an instant through electrodes placed on the head and hind limb does not seem to permanently damage the nervous tissues, for in one dog (No. 16) in which this was done and the animal allowed to recover from the anæsthesia, no change from his normal behavior was perceptible (the reflexes were normal; there was no paralysis, etc.).

Coming now to the question of variability in the strength of current necessary to cause death, we are convinced that this depends on the path through the body traversed by the current.<sup>2</sup> If the heart lies in this path, fibrillary contractions will result; if not so, only vagal inhibition. Currents passing between electrodes in the mouth and rectum necessarily traverse the heart and are always fatal. With the electrodes on the head and hind limb, on the other hand, most of the current will pass along the tissue about the spinal column and will frequently pass by the heart.

In several experiments we placed the electrodes on the head and anterior extremities, and invariably noted vagal inhibition of the heart, general convulsions, and respiratory cessation, but no delirium cordis. The respirations returned, and the heart started beating when the current was broken.

<sup>1</sup> American Journal of Physiology, 1898; vol. 1. p. 71.

<sup>2</sup> This explanation was first brought forward by Tatum (*loc. cit.*), and Cunningham, A Text-book of Legal Medicine and Toxicology, Philadelphia, 1903, p. 247.



In other experiments we placed the electrodes on the two anterior extremities, with results similar to those obtained in the previous cases, except in one dog in which fibrillary contractions followed the application of a current of 2300 volts for about ten seconds. Some of the current in this case had undoubtedly spread to the heart.

These observations seem to us to suggest a *possible prophylactic measure* for workers exposed to the danger of strong currents; viz., that they should wear a corset made of some conducting material; for example, copper. This corset, to be of any value, would require to be closely applied to the skin about the shoulders and base of the neck above, and to the lower portion of the trunk below; and opposite the cardiac region it would require to be separated from the skin by some non-conducting material—for example, India-rubber. It would certainly be of no use merely to wear such a corset separated from the skin along all its length by woollens, as, we are told, has been practised.

We are greatly indebted to the Cleveland Electric Illuminating Company for supplying us with the necessary current, and to Mr. E. E. Noble, their superintendent, who manipulated the apparatus for us.

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## THE PHYSIOLOGICAL RELATIONSHIP OF THE PROTEIDS OF THE BLOOD PLASMA.

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ALTHOUGH it is evident that there must be wide variations in the composition of the blood plasma even in health and that this variation must affect the proteid element of that fluid, still, owing to the great technical difficulties in the separation and estimation of these bodies, it is only within recent years that their study has been taken up vigorously, and so far the work on them has been almost entirely experimental, our knowledge of the subject not being sufficient to make it of clinical use. I was able to make the series of experiments on the variations of the proteids of the plasma under varying conditions, which form the basis of this paper, in the laboratory of Professor Franz Hofmeister, in Strasburg, whom I wish to thank for his constant help during the course of the investigations.

The separation of the proteids of the plasma was very inaccurate and unsatisfactory until the method of salting out was developed. This method is based on the fact that the addition of certain salts to solutions of proteids renders these insoluble. The various proteids of blood plasma are precipitated at different concentrations, and by adding varying amounts of certain salts at least four dis-

tinct bodies may be separated, viz: fibrinogen, euglobulin, pseudoglobulin, and serum albumin. The salts which are best adapted to the purpose are magnesium, ammonium, and sodium sulphates, and of these I selected the last, because it contains no nitrogen and all globulin is precipitated by half saturation, thus avoiding the necessity of adding dry salt. This salt reaches its highest solubility at 35° to 40° C., and therefore it is necessary to keep the solution constantly at this temperature and to do all filtering and other manipulations at the same. The sodium sulphate solution referred to in this article is one kept concentrated under these conditions.

These bodies after precipitation have previously been estimated by weighing of, or by determination of the nitrogen in, the precipitate. It seemed to me that it would be both easier and more accurate to determine the nitrogen in the filtrate and from this to calculate the amount in the precipitate, and my results have confirmed this opinion.

The method of preparing the body proteids from those of the food is still somewhat obscure, and it is uncertain whether each of the proteids of blood plasma arises independently or whether they are formed from a common mother substance—*e. g.*, serum albumin. The latter is made probable by the observation of Moll that serum albumin in the presence of sodium carbonate kept at a temperature of 56° C. for half an hour is partly converted into euglobulin and pseudoglobulin.

My experiments were performed with a view to throwing some light on this question.

We believed that if an animal were bled freely and then well fed, a comparison of blood drawn before and after the bleeding would show in the latter an increase of that proteid, if any, which stood nearest to the assimilation form. Also, that by starvation a relative decrease of the same form could be brought about.

The conduct of my experiments was as follows in all cases: The blood drawn by means of a glass cannula from an artery flowed directly into a measuring-glass which contained an amount of normal salt solution, plus 0.4 of sodium oxalate to prevent coagulation, equal in volume to the blood to be drawn. This mixture was immediately centrifugated and the clear plasma drawn off from the corpuscles. A specimen of this diluted plasma was measured off for nitrogen estimation; to a second specimen was added a quarter of its volume of sodium sulphate solution, to a third one-half, and to a fourth its own volume, a series of tests with gradually increasing amounts of sodium sulphate having shown that these concentrations lay between the limits of the globulins.

These mixtures were always made by adding the sodium sulphate solution to the plasma in a measuring-glass and filling up to a certain mark, thus avoiding contraction of the liquid. They were then poured into test-tubes which were stood in the same vessel of

water and kept at body temperature. The extractive nitrogen was estimated by further diluting the plasma with four times its volume of water and boiling. While boiling a few drops of a concentrated solution of zinc sulphate were added and the vessel removed from the flame. The solution of zinc sulphate is strongly acid and addition of too much, or prolonged boiling after addition, is likely to result in the formation of an acid albuminate. In such cases addition of sodium carbonate and boiling again has always given me a biuret free filtrate. The above precipitates were all filtered off and a measured amount of the filtrate taken for nitrogen determination.

All tests were carried out twice from the beginning, the precipitation being done separately and if the two did not agree well a third or fourth was made. In a few cases a control test was made with a much more dilute plasma and dilution was found to have no influence on the size of the precipitate.

The numbers obtained have been expressed as percentages of total proteid nitrogen. This avoids the disturbance from varying amounts of water in the plasma and shows better that in which we are especially interested, the relation between the different proteids.

Owing to the great variation in the percentage of globulin and especially of fibrinogen in different dogs, it is only possible to compare the results obtained from the same dog under varying conditions with each other. This makes a large series of bleedings necessary and limits the amount drawn each time to the least possible quantity.

In one of my last experiments I was surprised to find that although after standing at body temperature two hours there was a good precipitate of fibrinogen, after standing about five hours this had almost entirely disappeared. This was evidently the result of fibrinolysis, and the thought occurred to me that perhaps a partial process of the same nature might account for the very low numbers for fibrinogen which I have occasionally found. If this were so we would expect to find a large amount of albumin in the corresponding tests and this has always been the case. As the lysin would also be active in the euglobulin and pseudoglobulin precipitates, the small numbers for fibrinogen would not increase their apparent size. However, as this process is rather rare, it may generally be neglected.

1. INFLUENCE OF HEMORRHAGE. The animals were bled freely at intervals of several days and the blood thus drawn used for examination. The tables show the amount drawn each time and the interval as well as the results obtained.

It will be seen that in the dogs an additional proteid appeared which seemed chemically to be a nuclealbumin and which gave the plasma a turbid appearance. It was present from the first in the second dog but no cause for its presence could be seen. As this body is precipitated with the fibrinogen it increases the apparent

amount of that body and explains the increased amount found in the last column of the first series. A rough estimation of its amount showed that from 0.6 to 0.8 per cent. should be subtracted from the number given for fibrinogen. In the second dog it was more accurately determined.

#### EXPERIMENT I.—Dog, weight 7.2 kilograms.

	Date.				
	Nov. 23.	Nov. 26.	Nov. 30.	Dec. 7.	Dec. 14.
Cubic centimetres of blood drawn	145	72	80	108	75
Total nitrogen in 100 c.c. plasma	1.162	1.093	0.947	0.810	0.767
Fibrinogen (+nucleoalbumin)	17.7	10.7	9	16(9)	13.7(7)
Euglobulin . . . . .	8.2	12.3	19	24	17.3
Pseudoglobulin . . . . .	48.5	28	14.5	20	22.4
Albumin . . . . .	25.6	49	57.5	40	46.6

#### EXPERIMENT II.—Dog, weight 3 kilograms.

	Date.			
	Feb. 17.	Feb. 22.	Feb. 24.	Feb. 26.
Cubic centimetres of blood drawn	150	75	75	75
Total nitrogen in 100 c.c. plasma	0.676	0.824	0.865	0.764
Nucleoalbumin . . . . .	5.5	9	9.7	7
Fibrinogen . . . . .	2.4(17.4)	14	7.8	6
Euglobulin . . . . .	13.5	12	12.7	11
Pseudoglobulin . . . . .	19.3	21	21.5	20
Albumin . . . . .	59.3(44.3)	44	48.8	56

The first column here varies so widely from the normal that its value must be somewhat discounted, but if we suppose the presence of fibrinolysis and subtract, say, 15 per cent. from the albumin and add it to the fibrinogen the series seems much like the one above.

#### EXPERIMENT III.—Rabbit, weight 1.5 kilograms.

	Date.			
	Feb. 5.	Feb. 9.	Feb. 15.	Feb. 19.
Cubic centimetres of blood drawn	30	30	30	30
Total nitrogen in 100 c.c. plasma	1.048	0.789	0.737	0.767
Fibrinogen . . . . .	13	10.5	10	8.7
Euglobulin . . . . .	16	7.5	11.5	11.5
Pseudoglobulin . . . . .	11	18	14.5	18.3
Albumin . . . . .	60	64	64	61.5

Burckhardt, determining the globulin by dialysis, found in rabbits an increase of total globulin after hemorrhage, a result which does not agree with mine, although his method was too inaccurate for his results to have any great value. The most striking change in the blood, which I have found, is the steady and rapid fall in the per cent. of fibrinogen, although the rise in the albumin was almost as marked, especially in the dogs.

2. INFLUENCE OF STARVATION. The dogs used for this experiment were first kept for two days without food and then placed on half the quantity of meat necessary to retain nitrogen equilibrium. After several weeks of such hunger they were given unlimited quan-

tities of meat or bread, the tables giving the quality and quantity of food. An error in the estimation of fibrinogen made it necessary to state this with the euglobulin.

EXPERIMENT IV.—Dog, weight 10 kilograms.

	Date.			
	Dec. 20.	Jan. 5.	Jan. 13.	Jan. 25.
Diet . . . . .	Normal.	2 wks. $\frac{1}{2}$ diet.	3 wks. $\frac{1}{2}$ diet.	12 days meat freely.
Total nitrogen in 100 c.c. plasma .	0.784	0.702	0.946	0.868
Fibrinogen and euglobulin . . .	18	41.5	32.5	38
Pseudoglobulin . . . . .	26	15	26.5	21
Albumin . . . . .	56	43.5	41	41

EXPERIMENT V.—Dog, weight 13 kilograms.

	Date.		
	Nov. 10.	Nov. 23.	Dec. 8.
Diet . . . . .	1 wk. $\frac{1}{2}$ diet.	3 wks. $\frac{1}{2}$ diet.	2 wks. bread freely.
Total nitrogen in 100 c.c. plasma .	1.454	1.240	1.184
Fibrinogen and euglobulin . . .	45	52	21
Pseudoglobulin . . . . .	22	14	13
Albumin . . . . .	33	34	66

EXPERIMENT VI.—Dog, weight 8 kilograms.

	Date.	
	Nov. 23.	Dec. 8.
Diet . . . . .	3 weeks $\frac{1}{2}$ diet.	2 weeks meat freely.
Total nitrogen in 100 c.c. plasma .	1.107	0.749
Fibrinogen and euglobulin . . .	26	23.5
Pseudoglobulin . . . . .	24	7.5
Albumin . . . . .	50	69

The results of these experiments show in agreement with Burckhardt, Wallerstein, and Levinsky that the percentage of albumin is decreased during hunger, and that the greater part of the loss is made up by the fibrinogen and euglobulin, the pseudoglobulin being more irregular.

SUMMARY. One of the most striking facts shown in the tables is the wide variation in composition of the plasma in apparently normal dogs. This may be due to diet or to diseases which are not sufficiently severe to show themselves—*e. g.*, mild intoxications or infections. It seems, however, that there is an attempt to retain the percentage of total nitrogen at about the same figure and this shows much less variation than do the various proteid bodies.

The fact that after loss of blood the percentage of fibrinogen falls seems to show that this body is replaced with greater difficulty than any of the others, while the increase in albumin points to this as the first stage in metabolic formation of proteid. The globulins seem more irregular in behavior. This relation is also upheld by the relative decrease in albumin during hunger as this body would not be replaced from the food as rapidly as under normal conditions. This increase in globulin, as well as the appearance of nuclealbumin after loss of blood, may, however, be due to the decrease

in total proteid in the plasma and the necessity of keeping it at about the same point, causing the withdrawal from the solid tissues of the body, of these proteids, in which they are especially rich.

It seems certain at least that albumin and fibrinogen do not arise in the same way and under the same circumstances, and the probability of the globulins being formed from serum albumin, either in the blood or elsewhere, perhaps by ferment action as Moll has proposed, is heightened by my results.

#### LITERATURE.

1. Burckhardt. Archiv. f. exp. Pathologie, Bd. xvi. p. 332.
2. Moll. Hofmeister's Beiträge, 1903, Bd. iv. p. 563.
3. Levinsky. Pfluger's Archiv, 1903, Bd. c. p. 611.
4. Vallerstein. Thesis, Strasburg, 1902.

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## THE INCIDENCE OF GASTRIC AND DUODENAL ULCER IN PHILADELPHIA.

WITH SPECIAL REFERENCE TO THE POST-MORTEM RECORDS OF  
THE PHILADELPHIA HOSPITAL.

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THE following figures from the analysis of the post-mortem records at Blockley (the Philadelphia Hospital) were undertaken at the request of Dr. Osler for Dr. C. P. Howard's paper on "The Incidence of Gastric Ulcer in America."<sup>1</sup> They were not, however, completed in time to be incorporated in that paper, so that I present them now as an additional side-light on this interesting subject. I entirely agree with Dr. Howard's statement that we cannot base accurate or conservative conclusions on data obtained from clinical observations, and for that reason have confined myself to autopsy records alone. The discrepancies in clinical figures are well illustrated in his paper, where he deals with the subject from that standpoint. To quote him: "The figures from Philadelphia are rather puzzling. The University Hospital returns, kindly furnished me by Dr. James Tyson, give 19 cases out of 3979 admissions, or 0.48 per cent. On the other hand, the Pennsylvania Hospital has a very much smaller percentage—*i. e.*, 0.13. This discrepancy cannot be accounted for by any apparent reason." (Unless one takes into consideration the acknowledged uncertainty of the diagnosis in many instances, and the wide opportunity this offers for clinical error.)

<sup>1</sup> Medical News, October 8, 1904.

"In Baltimore we meet with similarly anomalous figures. At the Johns Hopkins Hospital there have been only 70 cases of gastric ulcer out of 16,553 medical admissions for a period of about fifteen years. This gives a percentage of 0.42. which is below New York (0.44 per cent.), yet higher than Philadelphia (0.16 per cent.). But in striking contrast are the figures from St. Joseph's Hospital, Baltimore, giving 4 cases out of 3298 medical admissions, or only 0.12 per cent. This, then, gives for Baltimore a percentage of 0.37, very far below New York, and still farther below Montreal (0.92 per cent.), and Boston (1.28 per cent.). These figures are interesting, and, no doubt, in a sense, indicative of the relative frequency of gastric ulcer in the localities specified, but surely lacking in the accuracy of the post-mortem figures given subsequently in the same paper as follows:

## CLINICAL PERCENTAGES.

City.	No. medical admissions.	No. gastric ulcers.	Per cent.
Boston,	33,506	432	1.28
Montreal,	20,466	189	0.92
New York,	31,690	138	0.44
Cleveland,	3,427	13	0.38
Baltimore,	19,831	74	0.37
Philadelphia,	43,709	72	0.16
Chicago,	3,930	6	0.15
Denver,	5,040	6	0.12
Total,	161,599	930	0.57
Breslau and Zurich.			0.66 per ct.
London . . . .			0.78 "
Berlin . . . .			1.33 "
Edinburgh . . .			2.02 "

## AUTOPSY PERCENTAGES.

City.	No. autopsies.	No. gastric ulcers.	Per cent.
San Francisco,	551	13	2.35
Boston,	3,039	57	1.84
New York,	561	8	1.42
Philadelphia,	826	10	1.21
Montreal,	3,153	33	1.04
Cleveland,	433	4	0.92
Baltimore,	2,223	19	0.85
Total,	10,341	144	1.32
London . . . .			4.6 per ct.
Europe . . . .			5.54 "

The great difference in the total number of autopsies in the several cities strikes me as also being probably a source of fallacy in calculating the absolute and relative frequency of ulcer in the different localities. In some instances, notably in the case of San Francisco, New York, and Cleveland, they seem to me too small in the aggregate to base a fair average upon. All such figures are, however, distinctly valuable, and bear out Dr. Howard's conclusions—*i. e.*, "1. Both clinically and pathologically ulcer is less frequent in America than in London and on the Continent. 2. That both clinically and pathologically ulcer is more common in the northeastern than in the more southern regions of America, with the exception of San Francisco."

Militating against the view expressed above—*i. e.*, of using post-mortem records only, are the opinions of Mayo,<sup>1</sup> who thinks that acute gastric ulcer is by no means as rare as it is usually considered. He says that it must be recognized clinically, for it usually heals, and the treatment is purely medical. "It is

<sup>1</sup> Medical News, April 16, 1904.

altogether probable," he says, "that the vast majority of acute ulcers heal, but a considerable minority fail to do so and constitute a share of the chronic ulcers. A chronic ulcer is frequently, if not usually, chronic from its inception."

If it is true that the "vast majority" of acute ulcers heal, then the objections raised to the results of post-mortem study on this subject by Byron Bramwell should also be mentioned. He thinks that acute ulcers often leave no scars and are not discovered at autopsy, or the scars if present are slight and often overlooked, so that a certain number of ulcers are overlooked in post-mortem statistics. Admitting the likelihood of these fallacies in acute ulceration, I still consider autopsy records the much surer way of computing the absolute and relative frequency of gastric and duodenal ulcers, certainly of the chronic forms.

The generally accepted causes for gastric ulcer are anæmia, hyperchlorhydria, certain occupations like shoe-making and tailoring, mechanical injury, the grinding action of the pyloric end of the stomach (Mayo), chlorosis and menstrual disorders, embolism and thrombosis (Virchow), as in heart disease or continued vomiting, superficial burns, and lastly (and often rather casually mentioned), nephritis and tuberculosis. It will be seen from the statistics below that the great majority of these ulcers (which we must consider as the chronic forms) are associated with some chronic dyscrasic disease, as, for instance, nephritis or tuberculosis.

It will be seen in the accompanying cases that in almost if not quite every instance there was an associated condition (in 0.76 per cent. of the cases nephritis or tuberculosis), to which in some manner we must consider the ulcers, usually multiple, etiologically related. So that I feel these two factors, nephritis and tuberculosis, should be emphasized more emphatically in text-book descriptions of gastric ulcer than is usually done.

In this connection, it would be interesting if we knew more about the relation of the stomach to chronic nephritis. Very little investigation has been done in regard to the perversions of gastric function in this relation, though such perversions are relatively frequent in nephritis. The investigations of Biernacki<sup>1</sup> seem to show that the secretion of gastric juice is in general reduced in all cases of inflammation of the kidney. Occasionally hydrochloric acid was absent, especially in severe cases of nephritis, during the stage of œdema, while it was present in milder cases, in large or small quantities. The secretion of pepsin was reduced, even in mild cases, while the motor power of the stomach was frequently found increased, not only in mild cases, but also in old chronic cases. He thinks that the glandular function is inhibited by toxic metabolic products, and that organic changes take place in the stomach in those cases in which

<sup>1</sup> Centralbl. f. klin. Med., 1890, Berliner klin. Wochenschrift, 1891.



nephritis has persisted for a long time and in which the blood changes are considerable and the nutrition of all the tissues has suffered. It may well be that one of the results of this perversion of function is the chronic gastric ulcer.

Since the time of Cruveilhier<sup>1</sup> (1835), who first recognized this condition, there have been numerous and classical reports upon gastric and duodenal ulcer, both in France and Germany. Rokitansky<sup>2</sup> (1839) and Jaksch<sup>3</sup> (1843) published careful studies in relation to gastric ulcer, while Krauss<sup>4</sup> (1865), Chvostek<sup>5</sup> (1882), and Oppenheimer,<sup>6</sup> (1891) have done the same in relation to duodenal ulcer. Indeed, following Cruveilhier's description, there have been in Europe, particularly Germany, an almost continuous series of experimental studies and reports contributing to our knowledge of these interesting morbid conditions. The foreign literature upon the subject is now enormous.

This has not, however, been the case in America, and accurate figures gleaned from autopsy records, while slowly making their appearance, as in Dr. Howard's valuable paper, are still all too scanty. So that any data, however inconsiderable, should, I feel, be welcome to those interested in scientific medicine.

LIST OF PATIENTS ADMITTED TO MEDICAL DEPARTMENT OF THE PHILADELPHIA HOSPITAL (BLOCKLEY) FROM JANUARY 1, 1893, TO DECEMBER 31, 1902 (INCLUSIVE).

(Vols. 16, 17, 18, 19, 115½, 116.)			(Vols. 116, 126, 127, 128, 133, 152, 153.)		
Men's Medical Ward, 1893 . . .	1524		Men's Medical Ward, 1893 . . .	1358	
" " " 1894 . . .	1506		" " " 1899 . . .	1399	
" " " 1895 . . .	1568		" " " 1900 . . .	1545	
" " " 1896 . . .	1475		" " " 1901 . . .	2013	
" " " 1897 . . .	1254		" " " 1902 . . .	1809	
	<u>7827</u>			<u>8,124</u>	
			End of ten years . . . .	15,451	
(Vols. 124, 125.)			(Vols. 124, 125, 157.)		
Men's Alcoholic, 1893 . . . .	517		Men's Alcoholic, 1898 . . . .	720	
" " " 1894 . . . .	460		" " " 1899 . . . .	710	
" " " 1895 . . . .	396		" " " 1900 . . . .	1002	
" " " 1896 . . . .	497		" " " 1901 . . . .	978	
" " " 1897 . . . .	515		" " " 1902 . . . .	989	
	<u>2355</u>			<u>4399</u>	
			End of ten years . . . .	6784	
(Vol. 120.)			(Vol. 154.)		
Men's Detention, 1893 . . . .	369		Men's Detention, 1898 . . . .	386	
" " " 1894 . . . .	338		" " " 1899 . . . .	424	
" " " 1895 . . . .	395		" " " 1900 . . . .	508	
" " " 1896 . . . .	363		" " " 1901 . . . .	574	
" " " 1897 . . . .	368		" " " 1902 . . . .	502	
	<u>1833</u>			<u>2394</u>	
			End of ten years . . . .	4227	

<sup>1</sup> Anatomie Pathologique, 1829-1835, vol. i.; Revue médicale, 1835; Arch. gén. de méd., 1855.

<sup>2</sup> Oestreich, Jahrb., 1839.

<sup>3</sup> Prague Vierteljahrsschr., 1843.

<sup>4</sup> Das perforirende Geschwür in Deutsch, Berlin, 1865.

<sup>5</sup> Wien. med. Jahrb., 1883.

<sup>6</sup> Mang. Diss. Wurzburg, 1891.

(Vol. 123.)				(Vol. 155.)			
Men's, Colored,	1893	. . . . .	162	Men's, Colored,	1898	. . . . .	192
"	"	1894	149	"	"	1899	183
"	"	1895	193	"	"	1900	182
"	"	1896	201	"	"	1901	279
"	"	1897	183	"	"	1902	289
			888				1125
				End of ten years . . . . .			
							2013
(Vols. 66, 66½, 106, 113.)				(Vols. 113, 136, 139.)			
Women's Medical,	1893	. . . . .	468	Women's Medical,	1893	. . . . .	562
"	"	1894	562	"	"	1899	621
"	"	1895	558	"	"	1900	699
"	"	1896	536	"	"	1901	734
"	"	1897	475	"	"	1902	680
			2629				3296
				End of ten years . . . . .			
							5925
(Vols. 82, 111.)				(Vol. 139.)			
Women's Detention and Drunk,	1893		313	Women's Detention and Drunk,	1898		424
"	"	"	1894	"	"	"	1899
"	"	"	1895	"	"	"	1900
"	"	"	1896	"	"	"	1901
"	"	"	1897	"	"	"	1902
			1686				2577
				End of ten years . . . . .			
							4263
(Vols. 82, 111.)				(Vol. 139.)			
Women's, Colored,	1893	. . . . .	56	Women's, Colored,	1898	. . . . .	96
"	"	1894	62	"	"	1899	92
"	"	1895	76	"	"	1900	101
"	"	1896	83	"	"	1901	116
"	"	1897	70	"	"	1902	127
			347				532
				End of ten years . . . . .			
							879

Making a grand total of 39,542 cases in ten years.

Cases of gastric or duodenal ulcer coming to autopsy during this time:

1. (Vol. vi., p. 241.) Ulcer in duodenum,  $\frac{1}{2}$  cm. in diameter, with thick white edges; 8 cm. from pylorus; tuberculous ulceration of intestine; male, white, aged thirty-five years.

2. (Vol. vi., p. 244.) Small healed ulcer in stomach over pylorus, with a deposit of pigment,  $\frac{1}{2}$  cm. in diameter; interstitial nephritis and fatty heart; male, white, aged thirty-two years.

3. (Vol. vi., p. 262.) Along lesser curvature there are several small superficial ulcers in stomach; tuberculous ulcers in œsophagus and intestines; tuberculosis of both lungs; male, black, aged twenty-three years.

Vol. vi., from January 1, 1893, contains 53 autopsies.

4. (Vol. vii., p. 29.) Stomach shows scars of old ulcers; interstitial nephritis; female, white, aged fifty-five years.

5. (Vol. vii., p. 53.) Stomach shows a few very small ulcers; tuberculosis of lungs and intestines; male, black, aged eleven years.

6. (Vol. vii., p. 108.) Stomach shows not less than a dozen bodies in the mucous membrane resembling tubercles, which have under-

gone ulceration; miliary tuberculosis; male, white, aged thirty-two years.

7. (Vol. vii., p. 183.) Duodenum shows minute swelling and ulceration of solitary glands and at some points hemorrhage; miliary tuberculosis of right lung; parenchymatous nephritis; male, white, aged fifty-three years.

8. (Vol. vii., p. 203.) Cup-shaped ulcer of pyloric end of stomach; chronic parenchymatous nephritis; female, black, aged forty-two years.

9. (Vol. vii., p. 269.) At the pylorus and within the valve there is an ulcer on the lesser curvature and anterior surface about one and one-half inches in diameter; carcinoma of stomach, liver, lymph glands; female, white, aged thirty-seven years.

10. (Vol. vii., p. 270.) Numerous small ulcers in the stomach, toward the pyloric end, and also in the duodenum; hypertrophy and dilatation of heart; male, white, aged sixty-four years.

Vol. vii. contains 286 autopsies.

11. (Vol. viii., p. 60.) About 5 cm. from pylorus and on greater curvature there are some small ulcers about 2 cm. in diameter; miliary tuberculosis; male, black, aged twenty-three years.

12. (Vol. viii., p. 93.) There is an old cicatrix on lesser curvature, midway between œsophageal and cardiac orifices; interstitial nephritis; atheroma; female, white, aged fifty-six years.

13. (Vol. viii., p. 101.) There is a small ulcer in stomach; interstitial nephritis; female, white, aged forty-four years.

14. (Vol. viii., p. 274.) A healed ulcer in posterior wall of stomach, 10 cm. from lesser curvature and 5 cm. above pylorus; scirrhus carcinoma of pylorus; female, white, aged fifty years.

Vol. viii. contains 297 autopsies.

15. (Vol. ix., p. 8.) Stomach contains three small ulcers, round and clear cut; one, 9 mm. in diameter on anterior surface near pylorus, perforating; a similar one at other extremity on median and posterior aspect, and a third on the interior surface, 4 cm. from last one, 11 mm. in diameter; chronic bronchitis; chronic gastritis; male, white, aged fifty-eight years.

16. (Vol. ix., p. 123.) Upon posterior surface of stomach, just above pyloric opening, there is a large perforating ulcer with raised indurated edges; carcinoma of stomach; male, white, aged fifty-four years.

17. (Vol. ix., p. 259.) There are multiple round ulcers in stomach and duodenum; perforating ulcer of duodenum; atelectasis of left lung; male, white, aged twenty-seven years.

18. (Vol. ix., p. 278.) There is a large ulcer in stomach a little behind and below pyloric orifice; interstitial nephritis; male, black, aged fifty-five years.

Vol. ix. contains 297 autopsies.

19. (Vol. x., p. 16.) There are ulcers in stomach varying in size

from a pinhead to a pea; miliary tuberculosis; male, white, aged sixty-three years.

20. (Vol. x., p. 92.) Duodenum is ulcerated; interstitial nephritis; female, white, aged sixty-seven years.

21. (Vol. x., p. 147.) On greater curvature there is a circular ulcer, 1 cm. by  $\frac{3}{4}$  cm.; it is in posterior wall nearer to cardiac than to pyloric end, and is crater-like, with indurated edges; tuberculosis of lungs; chronic nephritis; female, white, aged twenty-seven years.

22. (Vol. x., p. 219.) There is a small, round ulcer, with well-defined margins, in greater curvature of stomach; parenchymatous nephritis; myocarditis and endocarditis; female, black, aged twenty-one years.

Vol. x. contains 311 autopsies.

23. (Vol. xi., p. 144.) On lesser curvature, on anterior aspect of stomach, there is a round ulcer, 1 cm. in diameter, which has nearly perforated; parenchymatous nephritis; gangrene of lungs; male, white, aged twenty-five years.

24. (Vol. xi., p. 286.) There is a small, round, superficial ulcer in stomach; gangrenous stomatitis; diphtheritic gastroenteritis; female, white, aged ten months.

25. (Vol. xi., p. 295.) There is a small ulcer in the duodenum; enterocolitis; female, white, aged three years.

Vol. xi. contains 310 autopsies.

26. (Vol. xii., p. 55.) Near the cardiac end in relation to the lesser curvature there is an ulcer which measures  $\frac{1}{2}$  cm. in diameter, is cup-shaped, with slightly indurated edges; lobar pneumonia; female, black, aged twenty months.

27. (Vol. xii., p. 154.) On anterior surface near pylorus is an ulcer, 2 mm. by 3 mm., with irregular undetermined base; miliary tuberculosis; extensive superficial burns, eight to ten weeks old; chronic parenchymatous nephritis; female, white, aged thirty-eight years.

28. (Vol. xii., p. 176.) In neighborhood of fundus and extending toward greater curvature there are large ulcerations; the largest of these is probably 9 cm. to 10 cm. long and 8 cm. to 10 cm. wide; the ulcers tend to surround the cardiac end; the edges are ulcerated and thickened; tuberculosis of lungs; male, white, aged forty-eight years.

29. (Vol. xii., p. 262.) About 10 cm. from pyloric orifice in greater curvature there is a small, clear-cut ulcer, about 12 mm. in diameter; base clean, edges sharp cut; tuberculosis of lungs; acute nephritis; male, black, aged forty-seven years.

Vol. xii. contains 300 autopsies.

30. (Vol. xiii., p. 10.) On posterior wall about six inches from pylorus is a peptic ulcer about the size of a quarter of a dollar; chronic interstitial nephritis; female, white, aged seventy-six years.

31. (Vol. xiii., p. 19.) Stomach contains a few peptic ulcers of small size; chronic interstitial nephritis; male, white, aged sixty-eight years.

32. (Vol. xiii., p. 151.) Greater curvature shows a series of fine linear ulcerations arranged around œsophageal opening; these ulcers are about 4 mm. to 6 mm. in width; similar small ulcers are found in other parts of stomach; great anæmia; chronic nephritis; female, black, aged sixty-eight years.

33. (Vol. xiii., p. 169.)  $6\frac{1}{2}$  cm. from pylorus in anterior wall a large irregular oval ulcer is found, 5 cm. in length, opening in the long axis of the stomach; two more ulcerations, similar in character, but smaller, are noted; fatty degeneration of liver and kidneys; male, white, aged twenty-six years.

34. (Vol. xiii., p. 220.) 5 cm. from pylorus is a loss of substance, 1 cm. to 2 cm. in diameter; base of ulcer is smooth; edges ulcerated and sharply cut; arteriosclerosis; chronic nephritis; female, white, aged sixty years.

35. (Vol. xiii., p. 170.) Within 5 cm. of pylorus are four small ulcers, varying from 1 cm. to 2 cm. in diameter, with elevated edges; chronic nephritis; fatty degeneration of liver; female, black, aged fifty years.

36. (Vol. xiii., p. 185.) Pylorus is occupied by pigmented tuberculous ulceration, oval in form, 4 cm. to 5 cm. by 2 cm. in extent; base, granular; tuberculosis; female, white, aged seventy-four years.

37. (Vol. xiii., p. 267.) Along lesser curvature, within 5 cm. of pylorus, is found an area of ulceration, 4 cm. in diameter, borders elevated and indurated; base of ulcer is bile-stained; chronic nephritis; male, white, aged seventy-four years.

Vol. xiii. contains 302 autopsies.

38. (Vol. xiv., p. 1.) Stomach contains a large tuberculous ulcer as big as a quarter of a dollar, not far from pylorus; miliary tuberculosis; male, black, aged thirty-six years.

39. (Vol. xiv., p. 71.) Stomach is the seat of a chronic catarrhal inflammation, with ulceration and thickening of its walls; tuberculosis; chronic nephritis; female, white, aged sixty-one years.

40. (Vol. xiv., p. 234.) There are several small ulcers in stomach, the largest is about 1 cm. in diameter; interstitial nephritis; male, white, aged fifty-five years.

Vol. xiv. contains 300 autopsies.

41. (Vol. xv., p. 129.) There are superficial depressions in the mucous membrane of stomach, which may be healed ulcers; carcinoma of uterus; female, white, aged fifty-seven years.

42. (Vol. xv., p. 213.) About midway between cardia and pylorus are two or three small ulcers, the largest is about 8 mm. in diameter; they are shallow, with irregularly raised margins; miliary tuberculosis; female, white, aged thirty-one years.

Vol. xv. contains 297 autopsies.

Vol. xvi., up to January 1, 1903, contains 77 autopsies. No case of ulcer of either stomach or duodenum to date.

Total number of autopsies in ten years, 2830.

CONCLUSIONS. The following grouping shows the ulcers in relation to their apparent cause. Those in association with:

*Chronic Nephritis.* (2) 6.244; (4) 7.29; (8) 7.203; (12) 8.93; (13) 8.101; (18) 9.278; (20) 10.92; (22) 10.219; (23) 11.144; (30) 13.10; (31) 13.19; (32) 13.151; (33) 13.169; (34) 13.220; (35) 13.170; (37) 13.267; (40) 14.234. Total, 17; 16 gastric; 1 ((20) 10.92) duodenal.

*Tuberculosis, Miliary, or of Lungs.* (1) 6.241; (3) 6.262; (5) 7.53; (6) 7.108; (7) 7.183; (11) 8.60; (19) 10.16; (28) 12.176; (29) 12.262; (36) 13.185; (38) 14.1; (42) 15.213. Total, 12; 11 gastric; 1 (7.183) duodenal.

*Both Tuberculosis and Nephritis.* (21) 10.147; (27) 12.154; (39) 14.71. Total, 3 gastric.

*Chronic Bronchitis.* (15) 9.8; gastric.

*Pneumonia.* (26) 12.55; gastric.

*Atelectasis of Lung.* (17) 9.259; both gastric and duodenal.

*Carcinoma of Stomach or Elsewhere.* (9) 7.269; (14) 8.274; (16) 9.123; (41) 15.129; Total, 4; all gastric.

*Heart, Fatty.* (10) 7.270; both gastric and duodenal.

*Enterocolitis in Infants.* (24) 10.286; (25) 10.295; both gastric. (Extensive superficial burns, with tuberculosis and nephritis. (27) 12.154. Classified above under Tuberculosis and Nephritis.)

Grand total, 42; total gastric, 38; total duodenal, 2; both gastric and duodenal, 2.

In 20 out of 42 cases, or 47 per cent., the ulcers were multiple. Mayo says that in 20 per cent. of cases more than one ulcer is present. Brinton,<sup>1</sup> in 463 autopsies upon cases with ulcer of the stomach, found 57 with two ulcers, 16 with three or four, 2 with five, and 4 with more than five.

The sexes in the above series were equally divided, there being 21 males and 21 females, and the average age for the males was forty-three years, and for the females the same, a remarkably equal distribution. Welch, in his statistics, found 40 per cent. in males and 60 per cent. in females. The largest number of cases in his series occurred in males between thirty and forty years, and in females between twenty and thirty years, but there was much uniformity in the distribution in relation to the four decades. In my series the greatest number of cases occurred in males, 5, between fifty and sixty years, and in females, 5, between forty and fifty years. Here, too, there was a tolerable uniformity in relation to the four decades. Three of the cases were in infants, ten, twenty, and thirty-six months old, respectively. Dr. Osler mentions a case reported by Goodhart in an infant thirty hours old.

<sup>1</sup> Ulcer of Stomach, 1837.

It should be borne in mind in relation to these figures that the age given is the age of death and not the age of the incidence of the ulcer, which must be considered as occurring earlier.

In regard to size, Dr. Osler mentions an ulcer 19 cm. by 10 cm., reported by Peabody, as the largest one he knows of. The largest one in my series (No. 28) was 9 cm. to 10 cm. by 8 cm. to 10 cm. The same authority refers to a case reported by Berthold in which there were 34 small ulcers. Similar cases of multiple ulcers are seen in my cases Nos. 10 and 32 above.

It should be remembered in basing conclusions on the above figures that the lame, the halt, and the blind of the city's streets sooner or later find their way to the Philadelphia Hospital and Almshouse, and that it is pre-eminently the house of chronic invalidism and disease.

Dr. Joseph Walsh, late pathologist to the Henry Phipps Institute, tells me that during his term of service (1903) he made autopsies on 52 cases dying of tuberculosis of the lungs, and that in one case there were numerous small superficial ulcers in the stomach. Dr. Rosenberger, who followed him, says that during the year 1904 there were 55 autopsies, and no instance of gastric or duodenal ulceration.

To briefly recapitulate, the total number of medical admissions to the Philadelphia Hospital for ten years from January 1, 1893, to December 31, 1902, inclusive, was 39,542. The total number of autopsies was 2830. The total number of ulcers was 42, of which 2 were purely duodenal.

So that the summary, including the figures given by Dr. Howard for the Pennsylvania and University Hospitals, is as follows:

Hospitals.	Number of autopsies.	Number of gastric ulcers.	Percentage.
Philadelphia Hospital . . .	2830	40	1.41
Pennsylvania " . . .	547	7	1.28
University " . . .	279	3	1.07
Phipps Institute . . .	107	1	0.94
City of Philadelphia . . .	3763	51	3.15

## REPORT OF FIFTY CASES OF APPENDICITIS AND FIFTY CASES OF HERNIA WITH REFERENCE TO ALBUMINURIA.

By F. E. BUNTS, M.D.,  
OF CLEVELAND, OHIO.

In a paper read by Dr. John C. Munro before the American Surgical Association, in 1893, he calls attention to the significance of albumin and casts in surgical patients. It is particularly of interest

to note that he states that approximately 35 per cent. of all patients treated in the surgical ward showed signs of renal trouble. In concluding his paper he says: "We should expect evidence of renal irritation in over a third of the surgical cases found in a municipal hospital. The mere presence of a trace of albumin, with or without hyaline and granular casts, unattended by other evidence of renal damage, should not influence the prognosis in surgical disease or operation; and furthermore albumin and casts alone are apparently no contraindication to the administration of ether."

For some time my attention has been particularly drawn to the common occurrence of albumin and casts in the urine of appendicitis cases, so common, indeed, was this that I had been forced to feel that there was a definite relation between appendicitis and albuminuria and had in preparation a paper upon this subject. The statistics collected by Dr. Munro, however, made it appear that it was so common in all surgical cases that I concluded to take two classes of operations in which the peritoneum was opened, in one of which inflammatory processes were or had been present, and the other in which such was not the case. As a type of the first class I have taken 50 consecutive cases of appendicitis, and for the second class have selected 50 consecutive cases of hernia, none of which were the seat of inflammation.

These 100 cases may be summarized in the following manner: Appendicitis, 50 cases; of these, 43 were operated upon during the attack, and 7 between attacks, with 2 deaths. Examination of the urine showed albumin present in 18 cases previous to operation, disappearing after operation in 5 cases. Twenty patients who had previously been free from albuminuria developed it subsequent to the operation, making a total of 33, in whom it was present subsequent to operation.

Hernia (non-inflammatory), 50 cases; no deaths; of these, 11 showed albumin in the urine before operation, disappearing after operation in but 2 cases. Eleven new cases of albuminuria developed subsequent to operation, making a total of 20 in whom it was then present.

The number is obviously too small to have more than passing significance, and yet several interesting facts present themselves, and, should the collation of more numerous cases of a similar nature show similar results, might be of some value.

It may be said that these cases, with two or three exceptions, occurred in my service at Charity Hospital, and the examinations of the urine were made by one of the resident staff, assigned to that duty for four months at a time, and all doubtful examinations were subject to the approval or disapproval of the resident pathologist.

Referring to the tables, we find that of the inflammatory cases, 18, or 36 per cent., had albumin before operation, while of the non-



inflammatory cases, but 22 per cent. had albumin; 13, or 26 per cent., of the former had it both before and after, and 18 of the latter were similarly affected. Of the former, the albumin disappeared in 28 per cent. after operation, while in the latter it disappeared in but 18 per cent.

These observations, if they show anything, would tend toward the belief that intraperitoneal inflammation increases the frequency of the appearance of albumin in the urine in about 18 per cent. of cases; that operations in this class of cases cause the development of albuminuria in 40 per cent. of new cases, and an improvement or disappearance of albuminuria in 10 per cent.

In the non-inflammatory class, operations are followed by the development of new cases of albuminuria in but 18 per cent., and of disappearance of albumin in but 4 per cent. The smaller percentage cured by operation in the latter group suggests that the presence of albumin in non-inflammatory cases is more liable to be a permanent condition than in inflammatory cases.

It is a somewhat startling fact that 66 per cent. of all inflammatory cases operated upon had albuminuria subsequently, and 60 per cent. of these did not have albumin previous to operation. There is also a very decided difference between the percentage of albuminuria cases in inflammatory and non-inflammatory cases, both before and after operation. The statistics are very meagre, but they suffice to emphasize the observations in the paper already alluded to, that albumin is found in a very large percentage of surgical cases; that it cannot be considered on any ground yet established that it is of itself a contraindication to operation, for in the 100 cases here reported there were only 2 deaths, both acute suppurative cases, and among the cases of recovery from operation was a woman seven months pregnant, with albumin and hyaline casts, who was subsequently delivered of a full-term healthy child.

Unfortunately, there has been no systematic record kept of the condition of the urine at the time patients have left the hospital, so that no data can be offered at present as to the disappearance or continuance of the albumin and casts, but from records kept in a few scattered cases, I am of the opinion that a large number of them ultimately show no trace of kidney disturbance where such disturbance could originally reasonably be ascribed to the changes brought about by the surgical disease for which they were operated. While most of these cases have been operated under ether anæsthesia, it is a well-known fact that chloroform anæsthesia is followed not infrequently by the appearance of albumin in the urine.

IS THE TRANSPLANTATION OF THE CORD NECESSARY.  
IN THE RADICAL CURE OF INGUINAL HERNIA?<sup>1</sup>

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THE chief indication for the transplantation of the cord in the operative cure of inguinal hernia is the formation of a new canal and new rings in proper relation to each other.

The passage of the testicle in embryonal life, and, as a result, the presence of the cord necessitates a communication between the abdominal cavity and the scrotum. In order to prevent the escape of the abdominal contents through this opening, Nature has made the passage-way obliquely through the muscular walls of the abdomen; that is, with a deep ring above and internal and the superficial opening below and external, and these connected by a canal that contains the cord, but the lumen of which is normally obliterated by the apposition of the anterior and posterior walls. This obliquity, or the indirectness of the inguinal canal, is, perhaps, the chief factor in preventing the more common occurrence of rupture. When, for any reason, the intra-abdominal pressure is increased, this pressure is exerted at a right angle to the long axis of the canal, and has a tendency to hold the two walls in still closer relation and so help to prevent the formation of a hernia (Fig.1). This same valve-like action is seen naturally in the prevention of the regurgitation of urine by the oblique insertion of the ureter into the bladder, and artificially in the prevention of leakage after gastrostomy, and again, by the diaphragm after enterorrhaphy. Were it not for the obliquity the pressure would be parallel to the long axis, and would cause a widening of the canal and its openings (Fig. 2).

In practically all cases of inguinal hernia there is found to be a decrease in the obliquity of the canal and a widening of the rings, therefore, it has been reasoned that the radical cure will consist in the formation of new rings, and the construction of a new canal that will have the proper obliquity. This principle, including the transplantation of the cord, which we owe to the work of Marcy, Bassini, and Halsted, has been of the utmost importance in bringing the radical cure to that high standard upon which it now rests. Despite the improvements in the results that have followed these methods, there is still some dissatisfaction, as can be seen from the number of new or improved methods that have been submitted, for example, the method of Ferguson, which is based upon the relationship between the internal oblique muscle and the internal ring.

<sup>1</sup> Read at Colorado State Medical Association, Denver, October 6, 1904.

The deep or internal ring opens directly through the transversalis fascia, and under normal conditions is covered externally by the muscular structure of the internal oblique. With such circumstances, the attempt of any structure to pass through this ring will prove futile, because it will be forced back into the abdomen by the contraction of the internal oblique. In practically all hernias the internal oblique has been found to either completely or partially expose the internal ring, leaving the aponeurosis of the external oblique to counteract all increase of intra-abdominal pressure. Active contractile muscular tissue is certainly of more value in this respect than is fibrous tissue aponeurosis, even though this be distinctly attached to the muscle. Without this muscular check at the

FIG. 1.

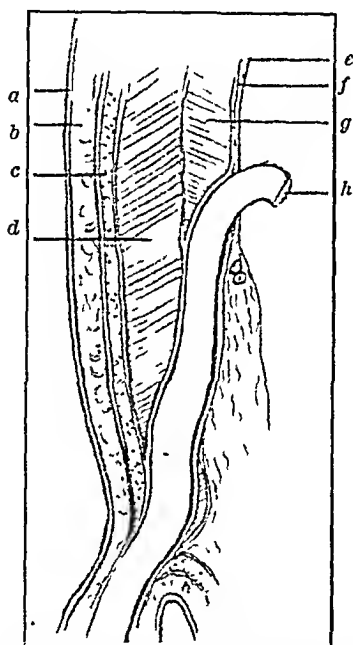
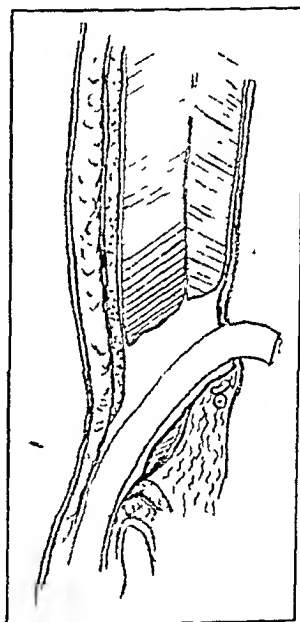


FIG. 2.



*a*, skin; *b*, subcutaneous tissue; *c*, external oblique muscle; *d*, internal oblique muscle; *e*, peritoneum; *f*, transversalis fascia; *g*, transversalis muscle; *h*, cord.

very onset of an attempt to force a passage, the canal is much more liable to be made patent by a gentle and gradual insinuation of omentum or intestine at the internal ring. Many operators have found the lower border of the internal oblique above the internal ring, but the majority of them have considered this to be the result of the protusion of the sac; but Ferguson looks upon this malposition of the muscle as a congenitally deficient origin of the internal oblique from Poupart's ligament, and as such, a cause, and not an effect, of the rupture. This view seems to be well substantiated by dissections and experiments upon the cadaver, while operations for the radical cure, based upon this theory, seem to be eminently satisfactory.

The transplantation of the cord seems to be considered by many as an unnecessary and objectionable detail, and in recent work there may be noted a widespread disregard for the older teachings, with a tendency to avoid interfering with the cord, and in operating to attempt to repair and strengthen the anterior wall of the canal instead of making the posterior strong at the expense of the anterior.

After the general adoption of the Bassini type of operation, Wolfier, in 1892, was, perhaps, the first to suggest that a radical cure might be effected without a transplantation of the cord. E. W. Andrews, in 1895, suggested such an operation, but did not recommend it. In June, 1899, Ferguson presented his method, which he had performed sixty-four times in the previous eighteen months. At this time he was very positive, and enthusiastically recommended that the cord be left in its normal situation. He said: "Leave the cord alone, for it is the sacred highway along which travel vital elements indispensable to the perpetuity of our race."

Bloodgood, in the same year, in his classic work on hernia, in the *Johns Hopkins Bulletin*, mentions a number of cases in which he did not transplant the cord, and suggests that in certain cases the cord be left *in situ*, and in others that the veins alone be transplanted, leaving the vas deferens in its normal surroundings and attachments. He said that after the removal of the veins: "The cord is then such a small affair that it is a question in my mind whether it is necessary to transplant it."

In 1900 Girard, and in 1903 Hoffman, suggested methods similar, in that the cord is not transplanted. And in August, 1903, Halsted, of the Johns Hopkins Hospital, presented a method strikingly similar to some of the above mentioned. This list of similar operations, devised independently, for the most part, shows that a breaking away from the typical Bassini procedure is at hand.

The objections, more or less real, to the transplantation of the cord may be stated as follows:

1. *An interference with the circulation and the function of the testicle.* Orchitis and epididymitis have followed the Bassini type of operation in a certain number of instances, even hydrocele and varicocele have followed in such a manner as to lead to the supposition that the operation served as a causative factor. These points are well covered by the statistics of Bloodgood, which show them to be rare in the hands of experts, but the fact that they occasionally occur, makes plausible the supposition that their occurrence in other hands is more frequent. But that such sequelæ do take place will seem quite reasonable when it is remembered that the mesocord is separated from its attachments, the cord torn from its natural surroundings, and, after being roughly manipulated, for a longer or shorter time, is placed upon different structures, sometimes a row of foreign bodies, such as silver wire or other suture material. The cord is subjected to additional and unusual traumatism in its new

and comparatively unprotected location. The muscular structures that were normally in front have been placed behind, depriving it of their protection and at the same time forming a strong bulwark, which acts as a counterpressure for any force from the outside.

2. *Strengthening the posterior wall at the expense of the anterior.* The aim of the majority of operators and of all those who employ the Bassini method seems to be the construction of a new canal which will have an exceedingly strong floor or posterior wall. It would seem just as rational to devote the same or less time and trouble in repairing the natural canal and in making the anterior wall or roof exceptionally strong. The procedure in both instances will be about the same; the internal oblique and the transversalis are sutured to Poupart's ligament in the one in front and in the other behind the cord. A fact well worth considering and not to be overlooked in comparing these locations is that Nature placed the internal oblique in front of the cord.

3. *The complexity of the operation.* When compared with the new methods, those which transplant the cord will be found to be more complicated and time consuming; they also necessitate more handling, and again, in consequence, a greater possibility of infection.

4. *Recurrence.* Recurrences of the hernia follow the Bassini type of operation, but since improvements in technique, such as rubber gloves, improved absorbable suture material, and Coley's suture above the cord, the percentage has become so small as to be practically disregarded. Recurrences have also followed operation of the new form, but these have been comparatively few, and a proper estimate of the percentage cannot as yet be determined. Such accidents will follow each and every mode of operating in variable small percentages for apparent reasons that cannot be discussed under this title.

It will be readily admitted that these objections to the transplantation of the cord are of slight and insignificant importance when compared with the cure of hernia. The problem may be summed up in the question: Is it necessary for the accomplishment of a cure of hernia to subject the cord to such manipulation and dislocation that the functional integrity of the testicle may be threatened? If so, further consideration is practically unnecessary, for the great gain, the cure of hernia, will far outclass any small loss, such as a remote possible interference with the testicle. But, if answered in the negative, then it is certainly far better to leave the cord in its normal situation.

The operation for the radical cure of hernia without interfering with the cord may consist of the following steps:

1. Skin incision.
2. Incision of the aponeurosis of the external oblique, with an exposure of the canal.

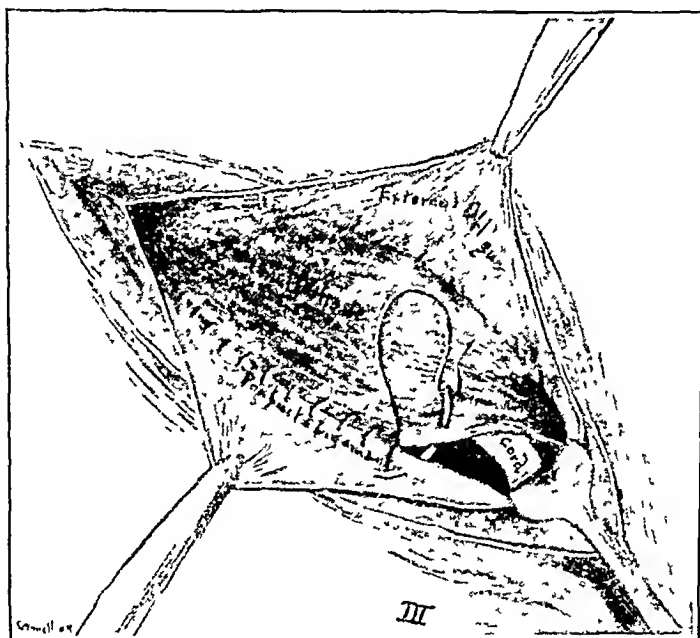
3. Dissection and removal of the sac, after the reduction of its contents.

4. Decreasing the size of the cord by the removal of the fat and veins if considered necessary. These steps are the same as in the usual operation for hernia.

5. Repair of the internal ring; the transversalis fascia may be brought together at the upper margin of the ring or the slack may be taken up below.

6. Suture of the internal oblique and the transversalis to the undershelfing of Poupart's ligament for its outer two-thirds, as seen in Fig. 3.

FIG. 3.



7. Suture of the aponeurosis of the external oblique. This may be done by an ordinary suture, which, with the above steps, comprises the "Ferguson typic operation."

The imbrication, or overlapping of the aponeurosis, as suggested by E. W. Andrews, with different variations and modifications, has been employed quite extensively of late, and apparently with great satisfaction.

It has aided in the compilation of the latest so-called Halsted operation of the Johns Hopkins Hospital, and is quite generally employed, whether the cord is transplanted or not. The imbrication of the external oblique aponeurosis is shown in Figs. 4 and 5. Another method of introducing this stitch, as shown by Andrews in the presentation of his method, is one in which the transversalis, the internal oblique, and the upper flap of the aponeurosis of the external oblique are all included in the loop of the stitch. This has the advantage of applying but one row of sutures to Poupart's ligament.

## 8. Closure of the skin.

The writer's experience has been confined to thirty-two case in which the cord was not transplanted, and the internal oblique sutured to Poupart's ligament according to the Ferguson technique.

FIG. 4.

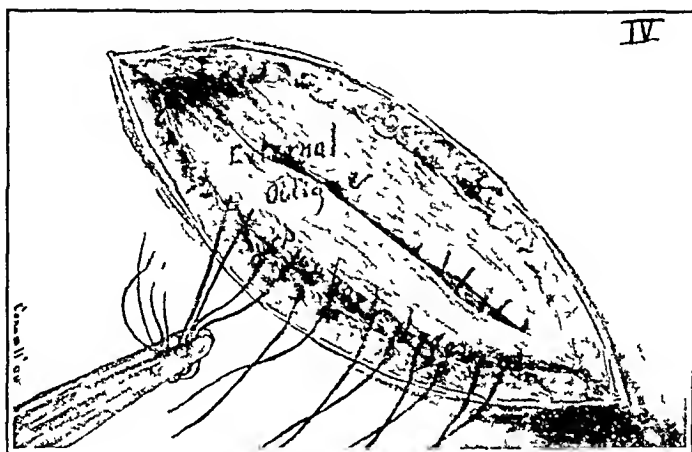
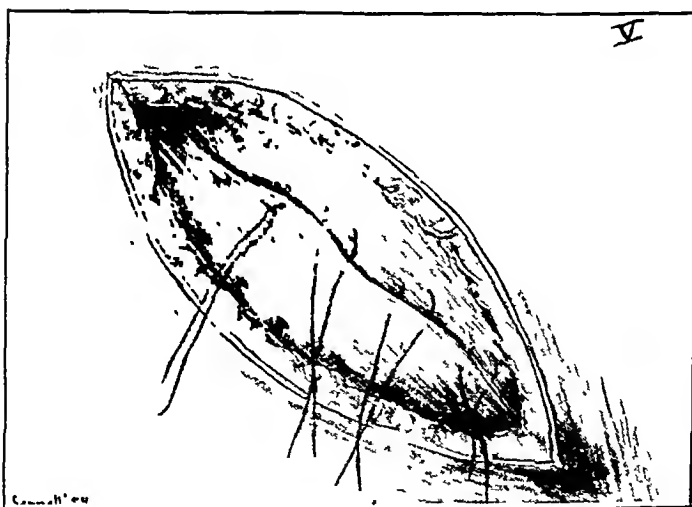


FIG. 5.



The external oblique was sutured in various ways. Of these, fourteen have been traced and heard from recently, two have had recurrence, but as one was complicated by an undescended testicle, and the other was operated upon for a recurrence after a Bassini operation, it would seem as though they would not serve as arguments against the method.

The object in presenting this short review of the subject is to submit it as a basis for a discussion of the question of the transplantation of the cord and to recommend the operation in which it is left *in situ*.

The great ease and simplicity, with the elimination of the danger of secondary changes in the testicle, are, perhaps, the more conspicuous reasons for its farther trial.

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## REPORT OF A CASE OF CHRONIC PYELITIS, DUE TO BACILLUS COLI COMMUNIS INFECTION, SIMU- LATING RENAL TUBERCULOSIS:

TREATED BY NEPHROTOMY, FOLLOWED BY THROUGH-AND-THROUGH  
ANTISEPTIC DOUCHES.<sup>1</sup>

BY LEWIS WHITAKER ALLEN, M.D.,

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THE following case is that of a woman coming to my service at St. Luke's Hospital, from the medical service of Dr. Evans, who presented a perfect clinical picture of renal tuberculosis. It illustrates to what extreme chronic infection of the kidney other than a tuberculous one may bring a patient.

The patient, Mrs. B., aged forty years, gave a negative family history. As a child she had had whooping-cough, but since then she had been free from contagious diseases. Has had a great deal of trouble, especially during the past few years, with her stomach and bowels. Her food digested poorly, giving rise to eructation, some pain, and occasional attacks of vomiting. Her bowels were persistently constipated. She had pain in the rectum and anus, giving rise recently to considerable distress. She had severe cystitis after the birth of her last child, five years ago. These symptoms recurred occasionally, and during the past two years have become at times very severe and troublesome. Her present illness dates back two years, during which time she lost strength and flesh. She has become continually worse since the beginning of the present year, complaining of pain in her right lumbar region, of almost constant difficulty and pain in micturition. She has been unable to digest any solid food for some time; has had numerous vomiting spells, almost constant distress and eructation of gas. During the past two weeks she has been unable to find anything which her stomach will tolerate. Previous to her admission to the hospital she has been having a temperature of 104° and over in the afternoon, according to the statement of her family physician, with sweating at night, and chilly sensations, though she has had no distinct chills.

On admission to the hospital the patient had a temperature of 99.4°, pulse of 80, respiration 18. During the five days of observation the temperature never rose above 100°. Examination on admis-

<sup>1</sup> Read before the San Francisco Academy of Medicine, July, 1904.



sion showed the patient to be very poorly nourished, very thin and emaciated, not much more than skin and bones. Heart and lungs negative. Marked tenderness over the whole of the abdomen, especially over the colon, most over the cæcum and sigmoid flexure. Epigastrium very sensitive. White blood count of 6600. She passed twenty-eight to thirty-six ounces of urine in twenty-four hours. It showed a specific gravity of 1014, acid, no sugar, faint cloud of albumin. Microscopically it contained a large amount of pus; no red blood cells. She was able to retain so little by mouth that rectal feeding was commenced. The urine was examined for the tubercle bacillus in vain. Fat was found in her stools to quite an extent. Five days after admission her ureters were catheterized. Pus was found in the specimens from both sides, but by far the largest amount came down from the right side. This was again examined for the tubercle bacillus, but none found. This was not considered proof against renal tuberculosis, as this so often happens with very serious tuberculous lesions of the kidneys. Culture from this urine gave a pure culture of the bacillus coli communis. At the time I considered this a contamination, although every precaution had been taken to obtain a pure specimen. Guinea-pigs were injected, but the patient was considered to be in such a critical condition that the usual wait of six weeks was considered inadvisable. The diagnosis of a tuberculous infection of the kidney was made without any reserve, because of the clinical picture. A disordered stomach, accompanied by vomiting, painful and difficult micturition, a painful and enlarged right kidney, urine from the pelvis of the kidney containing large amounts of pus, and especially, and most important of all, a thin and emaciated individual, showing systemic inroads upon the vitality of the patient through a chronic period of two to three years, made the diagnosis seem positive to us. Therefore, an operation was advised and undertaken.

An enlarged and congested kidney was exposed, which, after proper protection to the surrounding tissues, was split from top to bottom into the pelvis. My surprise was great, I assure you, to find no abscesses or other evidence of tuberculous infection. A culture was made from the pelvis of the kidney, a drain passed from the pelvis through the wound and the kidney drawn together with three or four catgut sutures. Another drain was placed below the kidney, and the wound closed. The culture from the pelvis of the kidney showed another pure culture of the colon bacillus. The guinea-pig, which had been previously been inoculated, died in five days of general purulent peritonitis, showing the pure culture of the colon bacillus, which pretty fairly completed the diagnosis of chronic pyelitis due to the bacillus coli communis with general chronic toxæmia of the individual.

The patient, soon after the operation, developed successively an infection of each of the salivary glands, which subsided under the

influence of ice. Her general condition almost immediately began to improve. Her stomach settled, and she was soon able to be put upon a liberal diet, gaining as much as ten pounds a week. After the third day I irrigated right through into the bladder with formalin, 1:2000, and peroxide diluted one-third, for three and one-half weeks. On removal of the tubes, the wound healed almost in a night, and within a week nothing remained to be dressed. In seven weeks after operation she was on her feet, and walked out of the hospital on the fiftieth day.

The tenderness of the kidney, evidently due as much to congestion as to infection, gradually subsided; the bladder irritation disappeared and the amount of pus in the urine diminished to a very small quantity, possibly coming from the opposite kidney. A culture from the wound, one and a half weeks after the operation, showed colon bacilli still present, but none were found after the third week, which determined me in removing the tubes and allowing the wound to heal.

The interest in this case lies in the general systemic intoxication produced by this infection, and the rapid response of the system to the thorough douching of the pelvis of the kidney and ureters with the antiseptic solution. The indications for the nephrotomy were clear, and the great benefit derived from the through-and-through flushing of the infected tract, according to well-founded surgical principles, bespeaks for this radical method a more frequent application.

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## GUNSHOT WOUNDS OF THE URETER; TWO CASES OF URETEROVESICAL ANASTOMOSIS.<sup>1</sup>

BY GEORGE TULLY VAUGHAN, M.D.,

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GUNSHOT wounds of the ureter are so exceedingly rare that I feel it to be my duty to report the case which fell under my care. In the history of surgery, so far as I have been able to ascertain, there has been recorded only one authenticated case of gunshot wound of the ureter, and that was the case of the archbishop of Paris, who was shot June 29, 1848. The ball entered the right lumbar region close to the spine. There was great depression, pale, anxious countenance, nausea, vomiting, intense pain in back and in the course of the sciatic nerves, and paralysis of the lower limbs. Urine flowed from the wound in great quantities and there was none in the bladder. An attempt to remove the ball was made

<sup>1</sup> Read at the Thirteenth Session of the Association of Military Surgeons of the United States.

without success and death occurred eighteen hours after the injury. A necropsy showed that the ball had passed through the third lumbar vertebra dividing the cauda equina just below its origin and the left ureter close to the pelvis of the kidney and lodged in the psoas muscle.

The doubtful case of Rayer reported by Hennen seems to have been a gunshot wound of the kidney. My case was as follows:

CASE I.—C. T., colored, male, aged thirty years, laborer, was admitted to the Emergency Hospital on account of an abdominal fistula which had followed a gunshot wound of the abdomen received October 3, 1903. The ball, a 0.32, entered about one inch to the inner side of the right anterior superior spinous process of the ilium and just below Poupart's ligament and lodged under the skin behind in the median line, having perforated or notched the fourth bone of the sacrum, whence it was removed.

A purulent discharge with symptoms of peritonitis followed and on October 11, my colleague, Dr. W. P. Carr, suspecting perforation of the bladder or bowel did an exploratory laparotomy in the median line. Numerous adhesions were found but no wound of the abdominal viscera. The wound was closed, with drainage in front, and in a week there was a purulent discharge in front through the opening for drainage and behind at the point of exit of the bullet, so daily through-and-through irrigation was used. The patient gradually improved, the discharge became thinner and looked almost as clear as water. On examination it was found to contain a little pus and a trace of urea. December 3, 1903, the patient was discharged recovered, with the exception of the fistula in front.

He was readmitted March 15, 1904 for the purpose of getting cured of the fistula, which had continued to discharge since leaving the hospital and kept his clothing constantly wet. A slight discharge also came from the posterior wound. The patient suffered no pain, ate and slept well, was well nourished and able to work. He voided from the bladder about 22 ounces of urine in twenty-four hours and from the fistula, judging from the amount collected for several hours, by means of a tube in the fistula, 2 ounces an hour or 48 ounces in twenty-four hours.

Examination of urine from the bladder gave the following result: reaction, acid; specific gravity, 1022; urea, 6 grains to the ounce; no albumin or sugar; a few pus cells. Fluid from the fistula appeared thin and slightly milky in color, reaction faintly acid; specific gravity, 1010; urea 1 grain to the ounce; pus cells abundant; a trace of albumin present. A probe could be passed into the fistula in front to the depth of four and three-quarters inches when it was arrested by a hard body, probably bone. Through the posterior opening the probe could be inserted to a distance of a little over two inches.

A diagnosis of wound of the right ureter was made and on March 19th the patient was operated on. The abdomen was opened along the outer border of the right rectus muscle and afterward the rectus was divided transversely just below the navel. The probe inserted through the anterior fistula was used as a guide but the operation was tedious and difficult on account of the numerous and strong adhesions of the intestines with one another and with the pelvic walls. The right ureter was finally exposed. It was found dilated to at least twice its normal size and was traced into a mass of unusually dense adhesions in the bottom of the pelvis. In attempting to free the ureter it was broken off at the location of the fistula as was shown by the appearance of the proximal end.

Nature was making a brave attempt to close the fistula, and incidentally the ureter itself, as at the site of the fistula the ureter was much contracted in calibre—being not larger than one-fourth or one-fifth of the dilated portion above. The result of this contraction was not only dilatation of the ureter but also probably damage to the kidney, as shown by the small percentage of urea found in the urine from the fistula. Sewing together the ends of the ureter (uretero-ureteral anastomosis) would have been almost impossible even if desirable, at this point, so ureterovesical anastomosis was decided upon. The bladder was opened in front and a small oblique opening was made through its posterior wall on the right side at a point considerably above the normal opening of the ureter. The end of the ureter was then split into two flaps about one-eighth of an inch long and drawn into the bladder by means of forceps introduced through the anterior and posterior openings. The flaps were spread open and stitched to the inside of the bladder by sutures whose knots were tied on the peritoneal surface of the bladder. The ureter was also sewed to the posterior surface of the bladder at its point of entrance. Very fine silk sutures were used. The anterior wound in the bladder was closed by two rows of continuous sutures—using first, catgut through all the coats, and second, silk, omitting the mucous coat and inverting the first row. The ends of the rectus muscle were united with heavy catgut, the longitudinal wound was closed with through-and-through silkworm-gut interrupted sutures and continuous catgut for the peritoneum and sheath of the rectus. No drainage for the peritoneal cavity, but a small piece of gauze was left projecting from the space in front of the bladder. A catheter was kept in the urethra several days to prevent distention of the bladder, but there was slight escape of urine from the anterior wound for a few days. The patient was discharged recovered April 19th. The urine was measured several times before the patient was discharged and was variable—running from 32 to 84 ounces in the twenty-four hours. April 17th Dr. F. R. Hagner reported as the result of a cystoscopic examination that the bladder mucosa was normal. The new open-

ing of the right ureter was seen as a small papillary mass from which urine flowed. A catheter was inserted into the old (normal) opening of the right ureter for about one and one-half inches beyond which it would not go. The scar in the front wall of the bladder was smooth.

The patient was again seen June 15th, about three months after the operation, when he appeared to be in perfect health.

CASE II. *Cancer of the rectum; inguinal colostomy; later excision of rectum and part of colon; right ureter divided; ureterovesical anastomosis.*—Mrs. E. T., white, aged forty-seven years; was operated on June 8, 1903, an inguinal colostomy being done on the left side, on account of ulceration of the rectum which had existed about a year and resisted all treatment. The patient's health improved after this operation and she gained in weight but continued to discharge pus and blood, so it was decided to remove the diseased rectum. March 14, 1904 this was done through the posterior wall of the vagina, but the disease was found to extend so high up the bowel, that the abdomen had to be opened and all of the rectum from just above the sphincter up to and including a portion of the sigmoid flexure was removed. In doing this the right ureter was accidentally severed near the bladder. The proximal end was split and sewed into the bladder exactly as in the former case.

There was no leakage so far as known either from ureter or bladder, and the patient made a good recovery and was discharged April 29, 1904.

Conservative surgery of the ureter may be said to date from the year 1877, when the first ureterovesical anastomosis was done by Tauffer. Previous to that time division of the ureter was usually treated by removal of the corresponding kidney, and even as late as 1893 we find Hermann Thompson stating that complete cure in lesions of the ureter is to be obtained only by removal of the kidney. He condemns grafting into the bladder or intestine as methods not to be recommended. Yet in the same year, sixteen years after Tauffer's case, we find the second successful ureterovesical anastomosis done by Novaro.

The next year, 1894, F. Westermarck performed the operation under the impression that his was the first successful case in the human being. Since then the enormous increase in the amount of abdominal and especially pelvic surgery has provided numerous occasions for the operation so that by 1903 Bovée had collected 111 cases of ureterovesical anastomosis, with seven deaths.

This operation is indicated whenever the lower part of the ureter has been divided or resected and the proximal end is long enough to reach the bladder. I believe it is to be preferred to any of the methods of uretero-ureteral union which have been suggested or practised for the following reasons given by Baldy:

(1) It is much easier to perform; (2) it is less likely to be followed by stricture, and (3) in case a stricture does form it is more accessible and easier to treat.

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## SCABIES IN THE UNITED STATES OF AMERICA AND CANADA.

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SCABIES is a disease assignable to the category of those which have been known since the earliest periods of antiquity. The contention that it is included with those designated under the title "Zaarith" in the Hebrew scriptures—a term which in the English translation of the Books of Kings and Leviticus has been rendered "leprosy"—is at least significant of a belief respecting its prevalence at an early period of the world's history. The literature which has accumulated on the subject of both the symptoms of its invasion of the human family and on the absurd errors which have been committed respecting its nature and effects is voluminous. Since the day when St. Hildegard first unmistakably referred to the acarid as its effective cause, and Bonomo and Cestoni, in 1787, presented their detailed description of the itch-mite, traversing the epoch when Hahnemann set forth his doctrines respecting the existence of "internal itch," as far as the hither side of the middle of the last century, when even distinguished physicians in France still doubted its origin in the encroachments of an animal parasite, the essays which have multiplied on the theme have been well-nigh innumerable.

Once the exact nature of the disorder established, its literature naturally contracted within channels. Volume One, for example,

of the Index Medicus furnishes but nine references to this subject in the medical literature of the world in all languages for the year 1903. Selecting at random single copies of half a dozen of the best known dermatological journals of this century, there is in all but a single abstract devoted to the same title—published in the *British Journal of Dermatology* for the year 1901.

The recent and unmistakable increase in the number of cases of scabies occurring in this country must be the excuse for again directing attention to a well-worn subject. The countries of North America have never been to a considerable extent the breeding-grounds of the *sarcoptes hominis*, even though at times the subject of frequent and well-sustained efforts at its colonization. This will appear the more singular if it be remembered that at the present day many of the cities of the United States and Canada vie with the capitals of Europe in the size of their populations and in the unwholesome crowding together of the unwashed classes in sleeping quarters and tenements.

There remains, nevertheless, a wide discrepancy in the comparison. The extent of the overcrowding of population in the larger towns of Europe is well illustrated in the most populous of them all, the metropolis of London. In the year 1901 the British census disclosed the fact that on an area of 117 square miles in that city more than four and one-half millions of people were bestowed. In the city of New York, the largest of the New World, there were fewer than three and one-half millions of people, in the year 1900, confined to an area of 326 square miles. "Greater London," with an area of 691 square miles, provides shelter for more than six and one-half millions of residents; while "Greater New York," which includes the population of Westchester County in the same State, and Bergen, Essex, Hudson, and Union Counties in the State of New Jersey, held only a few more than four and one-half millions of people on an area of 1258 square miles.

In this connection it is interesting to note that in the year 1870 and those immediately following, attention was attracted to the very large number of persons living especially in the Northern and Western States of this country, who were reported to be extensively affected with an "itch" supposed to be scabies. In some of the smaller villages and towns of the region mentioned it was said that every inhabitant was affected with the disease in question; and this irrespective of sex, age, or social condition. The affection was denominated "prairie itch," "winter prurigo," "frost itch," "winter itch," "swamp itch," and other names suggestive either of the State in which the disease prevailed, or of the lumbermen's camps where it also flourished. All attempts failing to recognize an efficient parasite in the production of the symptoms, it was finally shown that the affection was produced by the climatic changes, occurring often with marked severity in the northwestern

part of the country, in the autumn and winter chiefly, aggravated by the coarse clothing worn by many of the people, as well as by the use of cheap soaps, and often of parasitocides employed to secure relief from a fancied infestation. The patients presented all the evidences of extensively developed cutaneous pruritus, some even exhibiting vesicular lesions in the interdigital spaces, the features, however, in other points not closely resembling those of scabies. It was exceedingly difficult at the outset to persuade both physicians and patients that these were not instances of the "itch" or a similar contagious disease. It was noticeable that the disorder prevailed in the country as well as in the city, and that every man, woman, and child in certain communities was reported to be affected, a proportion never observed even where scabies is extraordinarily prevalent. During these years scabies prevailed in the northwestern part of the United States in a proportion scarcely greater than between 2 and 3 per cent. of all existing dermatoses.

The fruitful and unfailing source of scabies in North America is Europe, and in particular the crowded capitals of the Old World. Statistics showing the prevalence of the disease on the other side of the Atlantic are not available. Estimates, however, may be based on the annual reports of the out-patient departments of hospitals in England, France, Germany, Austro-Hungary, the Netherlands, and Italy, making it seem probable that on the lowest computation 25,000 cases of scabies are treated yearly in the capitals of these countries. It will appear probable in what follows that the number of cases of this disease seen in all the larger cities of North America in one year does not equal the number treated annually either in Vienna or Berlin, to say nothing of the larger totals represented in the statistics of London, or, more particularly, Paris.

The conditions favoring an increased colonization of the *acarus* on this side of the Atlantic are well known. These conditions are twofold and often related. The first requires an unusual increase in immigration to this country of passengers for the most part arriving in the steerage of transatlantic vessels; the second requires an unusual stimulus to the crowding together of the native-born populations of this country. At times these two conditions coexist; in other years the one may be effective without the co-operating influence of the other. It is also true that in different years the one may have a preponderating influence over the other. Stimulants to the crowding together of the native-born population are recognized in the desire of the people of the country to travel from their homes to visit great fairs, such as those opened in Chicago, San Francisco, and St. Louis, as a result of which enormous aggregations of human beings are housed for a brief time within relatively restricted limits. The vast army which Xerxes marched to Sardis has been exceeded in numbers by the visitors to one of these fairs on a single day.



Other stimulants to an unusual and extensive massing together of certain classes of the population of this country are the demands created by war. Here the crowding together of individuals, chiefly of the male sex, results in personal contacts which, by reason of the necessities of military life, are both intimate and imperative. Every one who has given attention to the subject understands that the casual contacts of hand-shaking, and even of the physical examination of patients made by physicians and students of medicine, rarely suffice to transmit scabies from an infested to a sound individual. Those are efficient contacts which become possible during the occupation of a bed in common, or those required when two individuals are engaged in toil seated closely to each other and exchanging articles during the hours of labor, with hands frequently touching; or those, again, common between mother and child, and between children at play together. These afford opportunities for the transference not of a male acarus only, or even of a single female, but of numbers of the young of both sexes, which are thus placed in a favorable condition for multiplication and colonization.

One of the earliest opportunities for the spread of scabies in North America was furnished by the exigencies of the War of the Revolution. At this period, when accurate statistics of disease are not available, proofs of the prevalence of scabies are found in the letters of officers of the Continental army and of civilians. These bear evidence of the degree to which many suffered during the war and for a time after hostilities ceased. A striking illustration of the difference between the people of that day and of this is furnished by the merchants, who are always ready to profit by the needs of sufferers. Of all remedies vaunted in the advertisements of the press of the present day for the relief of pruritic affections of the integument, few, if any, for the relief of "the itch" are pressed upon the attention of the public. Yet the daily journals of the larger cities of this country, as well as the shelves of the apothecary, during and soon after the War of the Revolution, bore witness to the number of secret remedies and nostrums for the cure of scabies.

The knowledge had to-day on the subject of the prevalence of scabies in North America is practically limited to the statistics furnished by the American Dermatological Association, compiled by its Committee on Statistics and published in annual reports of the Association from the year 1878 to the present time. These data have been accorded scant credence, both by some of the members of that body and by others not counted in its ranks, and this chiefly, if not wholly, by reason of the insufficiency of the returns, an objection obviously well grounded. The statistics of the Association are assuredly not those representing the frequency of skin diseases throughout the entire country, and certainly do not give the actual number of cases occurring in the cities from which the reports are

forwarded. They none the less possess an especial value of their own as indexes of the larger totals existing but never tabulated, and they have been greatly esteemed by those who have had occasion to refer to them, for they are the statistics collated exclusively by experts, who have agreed to reject from their lists cases not coming under their personal observation. Not only so, but they are furnished by men to whom the members of the medical profession not engaged in special practice have been pleased to send patients not falling within the lines of their own work. Further, they represent an experience in the largest cities of this country, and that an experience had in special hospitals and clinics, whither have resorted not merely patients afflicted with diseases of the skin, dwelling in such cities, but also those coming from adjacent smaller centres of population, many of whom, as is well known, naturally gravitate to the capitals where gratuitous aid is furnished. Lastly, with respect to the special affection here considered, it is well known that scabies, of all skin disorders, is most rife in populous centres, and probably occurs in a proportion of less than 2 per cent. of all dermatoses in the villages of the country. Exception, of course, is here made of the lumber- and mining-camps of the Northwest, and of the pseudo-towns which spring up in a day on the advance lines of a railway projection and which disappear as the iron parallels are pushed farther into a virgin territory.

The most serious flaw in the tables given below relates to the figures obtained from the city of New York, for in successive years represented in the compilation the returns from that city have not been made with equal fidelity and completeness. One of the reasons for this is to be found in the extreme difficulty of collecting the data from a large number of charities, widely separated in space the one from the other, many of them under different official management and with a non-coöperating staff. It is further to be noted respecting the tables appended that although the first statistics of skin disease ever collected in this country appear in the report of the committee published for the year 1878, no details are given in that year respecting scabies, the name not even appearing in the list. It will also be seen that the division of cases into public and private was not observed subsequent to the year 1887, the placing of all cases in one category after the date named being ordered by the Association in order to save contributors from the somewhat unpleasant necessity of reporting details giving a clew to the extent of their private practice. In the year 1891, further, it was determined that the statistical year should be changed from that extending from July 1st of one year to the thirtieth day of the ensuing June, to the twelve months represented in the calendar year. As a consequence, the figures for six months of the year 1891 are given, without itemization of the sources, at the foot of the column appended to the regular report.

The following table shows the number of cases of scabies reported from each of the cities named for each year of the period during which these statistics have been collated:

TABLE I.—CASES OF SCABIES REPORTED TO THE AMERICAN DERMATOLOGICAL ASSOCIATION.

Cities.	1878	1879	1880	1881	1882	1883	1884	1885	1886	1887	1888	1889	1890
Montreal	.....	.....	.....	.....	.....	8	39	.....	92	.....	127	76	7
New York	.....	14	35	64	76	132	52	36	178	.....	151	282	87
Brooklyn	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Boston	.....	35	29	22	67	96	179	24	334	34	494	368	254
Philadelphia	.....	9	13	11	30	25	.....	44	78	137	210	202	37
Baltimore	.....	.....	9	6	6	2	.....	8	8	24	24	.....	.....
Washington	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Chicago	.....	18	14	31	22	72	56	56	31	72	59	80	48
Cleveland	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Cincinnati	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
St. Louis	.....	.....	.....	.....	1	7	13	74	.....	36	27	28	.....
New Orleans	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
San Francisco	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Buffalo	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Private	.....	15	15	7	26	34	33	49	56	62	.....	.....	.....
Public	.....	61	85	127	181	308	306	393	668	581	.....	.....	.....
Total	.....	76	100	134	207	342	339	442	724	643	1092	1036	488
Total No. of cases of skin dis. collated	.....	8117	11,047	11,076	11,514	15,838	9329	14,007	14,984	10,366	15,165	18,166	6807
Cities.	1891	1891	1892	1893	1894	1895	1896	1897	1898	1899	1900	1901	1902
Montreal	9	.....	20	8	20	16	9	20	17	.....	8	10	15
New York	31	.....	578	304	413	82	13	213	245	257	227	125	490
Brooklyn	.....	.....	.....	.....	59	32	35	39	60	70	31	29	.....
Boston	392	.....	189	278	242	133	130	156	67	129	136	153	485
Philadelphia	.....	.....	310	123	146	61	35	.....	.....	90	5	15	135
Baltimore	111	.....	.....	.....	.....	.....	.....	94	116	104	.....	.....	75
Washington	.....	.....	.....	.....	.....	.....	.....	.....	.....	42	32	37	27
Chicago	97	.....	84	127	46	32	31	42	23	27	34	30	30
Cleveland	.....	.....	10	35	44	9	13	10	18	23	16	47	34
Cincinnati	.....	.....	.....	.....	.....	.....	.....	.....	.....	31	49	33	43
St. Louis	47	.....	.....	26	29	18	.....	5	14	54	6	25	32
New Orleans	.....	.....	.....	.....	.....	.....	.....	36	17	27	24	46	.....
San Francisco	.....	.....	.....	.....	.....	.....	.....	.....	20	.....	.....	21	19
Buffalo	.....	.....	.....	.....	.....	.....	.....	.....	.....	30	.....	.....	.....
Total	687	985	1191	901	999	383	266	615	583	897	568	373	1315
Total No. of cases of skin dis. collated	13,038	17,784	25,797	19,272	24,321	15,130	10,880	23,925	21,973	31,280	22,455	21,976	32,462

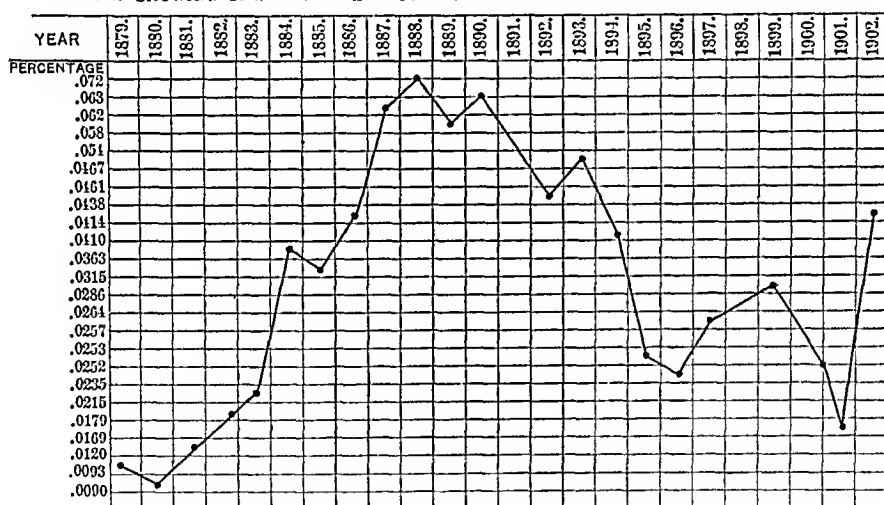
The total number of dermatoses collated in the statistics of the American Dermatological Association from the year 1878 to the year 1903, inclusive, is more than 440,000 (up to the year 1903 the figures were 439,552). This represents a population greater than that of either Washington, D. C., San Francisco, New Orleans, or Milwaukee, and is nearly that of Cincinnati and Los Angeles

combined, the figures being those taken from the last census. The total number of cases of scabies reported is about 16,000 (the figures at the last report, inclusive, were 15,526). This represents a population larger than that of Baton Rouge, La., or Annapolis, Md., and is very nearly that of the city of Rome, N. Y. For the entire period the proportion of scabies to all other dermatoses recognized in the Association lists is about 3 per cent.

In consulting the table it should be remembered that in successive years not only was the experience of each reporter enlarging, but the population also of the country, including that of the cities from which the returns were made, was furnishing a progressively larger area for observation. As time went on, the Association had occasion to enlarge its list of contributors by additions from several cities not represented in the earlier days of its organization.

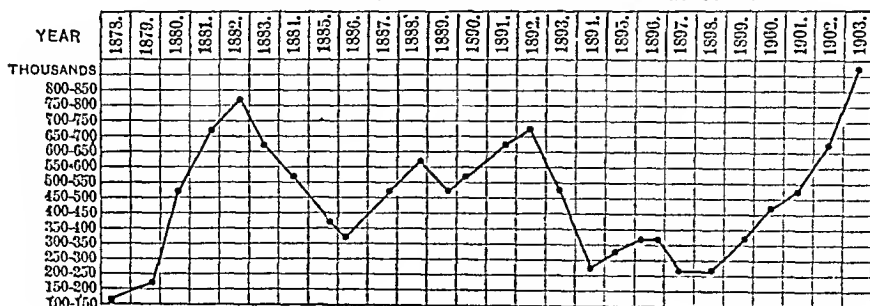
The following table represents the percentage of cases of scabies to each total number of cases of diseases of the skin reported for each separate year:

TABLE II SHOWING THE PERCENTAGE OF CASES OF SCABIES TO ALL OTHER DERMATOSES.



For the purpose of comparison, the following table is appended showing the number of immigrants arriving in this country from all others for each of the years named:

TABLE III SHOWING THE NUMBER OF IMMIGRANTS FROM ALL COUNTRIES REACHING THE UNITED STATES FROM 1878-1903 INCLUSIVE.



The first impression received from an examination of these tables suggests a relation to economic questions not pertinent to the subject under consideration. For example, the columns indicate with tolerable clearness the improvement of the social condition of our people following the resumption of specie payments in the year 1879, an improvement that continued for several years that followed; they point to a financial prosperity of the country at large, preceding the disastrous period between the years 1892 and 1896; they indicate a reduction in the number of immigrants when the Spanish War of 1898 doubtless withheld many from adventuring to a new land; and they significantly explain an enormous increase in the number of foreigners seeking these shores during the last three years of unparalleled prosperity.

If, however, one should expect to find the rise and fall in the scabies list correspond exactly with that of immigration, the result would be disappointment. A somewhat deeper insight into the significance of the facts throws light upon both the coincidence and the lack of coincidence in these separate waves.

First, it is to be understood that an increase in the number of cases of scabies in any community requires a certain period of time for transmission of the disease to it from another part of the country; and, also, in any given community for the spread of the disease among its members. The time required for this transmission on a large scale is not known; certainly, from several months to a year may be thus demanded. Evidence, however, is at hand that when circumstances are especially favorable but three months may be needed to ensure the result.

Beginning, then, with the year 1879, it is clear that the number of cases of scabies increases almost *pari passu* with the increase in immigration, even up to the year 1883, that is, a twelvemonth after the decline in immigration began, for the reason that the impulse of the wave, as suggested above, extends somewhat beyond the date of the first decline in the immigration-wave registered in 1882. The decline in the scabies wave, however, is distinct, as might have been anticipated, in the following year, viz., 1884, and doubtless resulted from the falling off in the number of steerage passengers reaching these shores at that time. The year 1888-1889 saw six new States added to the Union and the Territory of Oklahoma thrown open for the first time to white settlers. The push of the native population to these virgin lands was pursued by an immigration-wave in 1891-1892 that was not without influence upon the Eastern seaboard. The percentage of cases of scabies rose somewhat with the increased immigration of that period, declining in 1889 and increasing in 1890 from similar causes.

In the year 1893, however, there was a sudden and striking loss of parallelism in the waves, for it witnessed a marked decline in immigration, accompanied by a significant increase in the number

of cases of scabies reported. This was, without question, due to the crowds of native population flocking to the World's Fair in the city of Chicago. Naturally, the influence of this wholly unprecedented massing of the people in a Western State had an influence upon the scabies statistics not so fully perceived in the Eastern cities, which theretofore had enjoyed the unenviable and almost exclusive privilege of supplying the West with colonies of acari. In the following table the statistical returns for the year of the Chicago Fair of a group of Western cities are contrasted with the same from the cities of the East. The figures speak for themselves:

TABLE IV.—CASES OF SCABIES REPORTED TO THE AMERICAN DERMATOLOGICAL ASSOCIATION FROM EASTERN AND WESTERN CITIES.

Year.	Eastern Cities.	Western Cities.
1878 . . . . .	.....	.....
1879 . . . . .	58	18
1880 . . . . .	86	14
1881 . . . . .	103	31
1882 . . . . .	179	23
1883 . . . . .	263	79
1884 . . . . .	270	69
1885 . . . . .	312	130
1886 . . . . .	690	34
1887 . . . . .	535	108
1888 . . . . .	1006	86
1889 . . . . .	928	103
1890 . . . . .	385	48
1891 . . . . .	543	144
1892 . . . . .	1097	94
1893 . . . . .	713	188
1894 . . . . .	880	119
1895 . . . . .	324	59
1896 . . . . .	222	44
1897 . . . . .	522	98
1898 . . . . .	505	92
1899 . . . . .	692	192
1900 . . . . .	439	129
1901 . . . . .	369	202
1902 . . . . .	1177	158

The table indicates clearly that in the year 1888, the year of the addition of the new States and of the opening up of the new Territory, more cases of scabies were reported from Eastern cities than in any previous year, the number being nearly double that reported for the preceding twelvemonth; while for the year of the World's Fair, in Chicago, there was an actual falling off, 384 cases fewer than in 1892, the year preceding; while the Western cities reported an increase of nearly 100 over that of the previous twelvemonth, the number of cases exceeding by 44 the highest number ever previously reported by them.

In the year 1898 occurred the war with Spain. In the autumn of that year and during 1899 the number of cases of scabies increased coincidently with an increase in the number of immigrants. The Western cities promptly reported 100 cases of scabies above that of

the previous year, the total number being within four of that representing the increase during the World's Fair. The increase in the number of cases reported from the Eastern cities was precisely 87.

Having in view the supposedly careful examination of immigrants made under the direction of the General Government in the city of New York, where most of the immigrants to this country are landed, on a *priori* grounds it might be thought that the published reports of the Commissioner-General of Immigration would throw light upon the question considered in these pages. But the result is disappointing. The published report, for example, for the year 1903 (the last issued) indicates that but seven immigrants during the year were scabrous, a figure manifestly erroneous as to the fact. It is possible that the inspectors of immigrants are engrossed with more serious problems than those which concern the animal parasites. Every incoming steerage passenger is not stripped and physically examined, as are applicants for admission to a well-ordered hospital. It probably suffices the inspector if the patient be free from symptoms of tuberculosis or other of the graver forms of disease which it is sought to exclude. Lepers have passed immigration inspection not merely in this country when coming, but also when returning after a trip homeward. Not many years ago, a leprous patient from Sweden, with the evidences of his ailment written so broadly on his countenance that two experts who examined him pronounced without hesitation on his condition, twice passed successfully what is popularly supposed to be an efficient barrier erected by the vigilance of the inspectors. Is it not subject for wonder that numbers of cases of scabies annually traverse these barriers without detection or hindrance? But it would be indeed a subject for wonder if the number of cases of scabies occurring in immigrants to this country during one year examined in the city of New York, was actually only seven as officially reported.

The year 1904 recently concluded furnished the amplest opportunity for the spread of scabies in this country which the acarus family has hitherto enjoyed. Briefly, there was, first, the largest immigration this country has ever received from abroad; and, second, a great fair held in the city of St. Louis, collecting in unprecedented numbers in a single district of Missouri the native-born population of the country, if not from all, at least from a very large number of all the States of the Union. Judging from the data collected in past years, the number of cases of scabies in this country should soon exceed that ever before recognized in its history. Such will assuredly prove to be the fact. The statistical report of the American Dermatological Association for the year 1903 will soon be published. The tables include returns from twelve cities of the United States and Canada, showing that a total of 1743 cases of scabies has been recorded, a figure exceeding by 348 the largest number ever previously reported for one year from the same

sources. These are indications of the general spread of the disorder which are not without special significance.

For the first time in many years, scabies is developing in private practice. Between fifteen and twenty years ago, it was rare indeed that a case of "the itch" in this country occurred in the well-to-do classes of society consulting their family physician for relief of their ailments. If there is to be an unusual extension of scabies from the conjunction of the two co-operating causes cited above, the result should have begun to be apparent after about the middle of the summer, when most of the visitors to the Fair had had time to return to their homes and when the newly-arrived immigrants had had sufficient opportunity to distribute their uninvited guests in the communities where they concluded to settle. During the year 1904, my associates and I were applied to for relief of no fewer than 48 cases of scabies in private practice, the larger number between August and the last of December. Our clinical cases for the same year numbered 150, not a very large figure for the outpatient department of a clinic in a large city. But when it is noted that one-third of all the patients applied for relief during the last two months of the year, it will be seen that the number of cases under observation is beginning to indicate the operation of the agencies alleged to be effective.

It has been said, not without some basis of fact, that in this country soap is too cheap and water too abundant to permit of great extension of scabies in any region for any length of time. The truth is, that while there have been recognized here a few instances of the severe form of disease still described under the title of "Scabies Norvegica" (somewhat misleading for the reason that typical forms of extensive scabies as originally thus designated have occurred in the Northwest) a different type of "the itch" is now prevalent. This is confusing to practitioners who have been made familiar in a past experience with instances either of severe non-parasitic pruritus cutaneus, or of the old-time forms of scabies illustrated in the colored plates which are in the hands of so many members of the profession.

In these illustrations of the disease, as also in the well-marked features presented by patients whom American physicians studying abroad have seen in attendance upon the clinics of the capitals of Europe, the symptoms are so pronounced as to be practically unmistakable. The hands, for example, are usually tumid and well sprinkled with commingled vesicopustules, papules, crusts, scratch-marks, and the characteristic burrows of female parasites. Elsewhere the classical regions of involvement between the two parallels furnished above by the line traversing the nipples and below by that passing above the upper border of the patellæ, furnish a picture similar to that presented in the two hands, though often the evidences of scratching, with resultant excoriations and crusts, blood-



stained from the induced oozing, are exaggerated. The subjective distress, of which complaint is commonly loud, is considerable.

Now, the symptoms of this disease, as they occur in private practice, especially, and at this date when the disease is spreading even among the cleanly and well-to-do classes are those modified by the habits of the patients of this class with respect to the bath and the clothing. As to the latter, while it is true that no evidence is at hand showing that the itch-mites infest the clothing of patients (in some cities, such as Boston, the clothing of scabies patients is subjected to hot-air treatment for destruction of parasites; in others as in Paris, no such precautions are taken), still, among the cleanly, when the disease has once developed, soft and unirritating under-clothing contributes greatly to the comfort of the sufferer. It will be remembered that the class of people to whom reference is here made includes those occupying their own homes, those accustomed to the daily tub, those comfortably clad, those scrupulously careful as to the person, those who often may well be described as given over to frenzied anxiety respecting contamination and filth accumulation.

When persons of this class, actually victims of scabies, confront the practitioner (with the classical types of that disease formulated in his mind), an error is almost inevitable on account of the character of the symptoms in evidence. All the interdigital spaces carefully searched reveal possibly but two or three faint lines, scarcely suggestive of a well-excavated cuniculus. Elsewhere the axillary regions, possibly of both sides, often of but one (the left, where the predominantly used right hand finds easier accessibility to the skin) present two or three ill-defined, faintly discolored, flattish macules or papules. In the case of male patients, even those best washed, one can generally find at least a single papulopustule involving the skin of the penis or (more rarely) the scrotum, a practically pathognomonic symptom when considered in connection with others presented. Women occasionally have a similar lesion about the nipple or around the umbilicus. In these cases the complaint of nocturnal distress is fully as eloquent as in others with more classical symptoms of the disease. The patients, it should be remembered, are wholly unaccustomed to the incursions of bugs, fleas, and lice, and they highly resent the species of bodily torment to which they are subjected. In the case of mothers and of children, a history of contagion or of involvement of other members of the family can often be obtained.

The incautious practitioner, viewing the symptoms as far removed from those of the disease which represents scabies to his educated mind, is inclined to believe that they are produced by commoner causes of pruritus ("uric acid," harshness of climate, "defective metabolism," etc.); but no relief will be secured before the treatment is directed to removal of the efficient cause. He is more dis-

posed to err in these by-ways of difficulty for the reason, as before explained in these pages, that in America scabies in private practice up to a recent date was practically unknown.

If the details to which attention is here directed point to any definite conclusions, they portend no general and formidable extension of the pest in this country. The number of sufferers both in private and public practice will gradually increase beyond any limit heretofore recorded, and then there will follow the usual diminution in the number of the infested until the figures of the average of years are reached. Then the tidal wave will return when the country is again buffeted by a huge billow of immigration or agitated by some cause which determines a large movement of population within its borders. Whether the ultimate opening of the Isthmian Canal, which is to be practically a water-way of the United States of America, will exert a similar influence it may be too early to decide. But the important practical lessons of the situation are sufficiently obvious.

*Ex uno disce omnes.* The significance of the facts related concerns more than one of the serious problems of public hygiene. However large the rewards of international commerce from the point of view of economics, certainly at the present day the price to be paid involves the health and comfort of the people. The virgin territory of the United States of America has been bombarded for two centuries, from the North, from the South, from the far East, and from the distant West, with intermittent volleys of germs of leprosy, yellow fever, bubonic plague, Asiatic cholera, and the less deadly missiles furnished by colonies of animal parasites. These all are advance corps of the great army of Diseases of the Filth. The physical welfare of the people of this country demands practical measures for their safeguarding, but none the less a national education, which shall demonstrate the necessities of the House Cleanly before those of the House Beautiful.

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## X-RAY TREATMENT OF CUTANEOUS EPITHELIOMA.

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AMONG the factors to be considered in estimating the value of the x-ray treatment of cutaneous epithelioma, the most important is the liability to recurrence, and it is in this very particular that our knowledge is most limited. The purpose of this paper is to add something to the recorded data bearing on this subject. The cases are taken from the private practice of Dr. L. Duncan Bulkley, to whom I am indebted for the privilege of reporting them. The

diagnosis was always clinical. Biopsies are generally difficult to obtain, and in many of the cases, moreover, would be equivalent to excision, and subject to the same objections as the latter.

Before giving the clinical histories, however, there are two minor points of technique which I would emphasize.

1. The distance between the tube and the lesion should be made as short as is consistent with the avoidance of sparking from the apparatus to the patient. In treating a large area, like an extensive psoriasis, this rule does not hold. With a small lesion, as is usually the case in epithelioma, it reduces the time of exposure very materially; for since the quantity of rays received on a given surface varies inversely as the square of the distance between that surface and the anode, it follows that an exposure of four minutes at four inches is equivalent to one of twenty-five minutes at ten inches.

2. The screen used to protect the normal parts need not be entirely opaque to the  $x$ -rays. I have used ordinary rubber sheeting, folded into three layers, and have repeatedly carried the treatment to the production of a moist dermatitis of the exposed area, while the parts covered by the shield remained entirely unaffected. This seems to show that the rays which affect the skin have very little power of penetration. The advantages of this material are the ease of manipulation and the avoidance of the disagreeable tingling so often noticed when lead is used.

CASE I.—Female, aged forty-one years. The disease began about the year 1890 as a small pimple on the left temple. This was burned a number of times but the disease progressed, and in January, 1903, the whole left temporal region was covered with scar tissue, with a number of pearly nodules and small crusted areas scattered over it. At the outer extremity of the left eyebrow there was a triangular ulcer about a quarter of an inch on a side, with hard, raised edges. Between January 12 and March 27, 1903, the lesion received twenty-seven treatments, aggregating two hours and five minutes. The reaction was never carried beyond redness and scaling, but the ulcer healed, and the crusted and pearly nodules all disappeared, leaving a smooth, pale scar. On September 6, 1904, the patient wrote that there was still no sign of recurrence.

CASE II.—Male, aged seventy-eight years. The disease appeared first in 1891 as a small pimple in front of the lower end of the right ear. It was treated with some caustic, but recurred and was removed by operation in 1898. There has been no recurrence at this site, but in 1900 a small, scaling nodule appeared in front of the left ear. This second lesion was treated with mild ointments, and alternately healed and recurred, still gradually increasing in size, until October, 1902, when there was a small epitheliomatous ulcer with a slightly bleeding base. This healed after a single exposure of five minutes, but recurred, and in May, 1903, the treatment was renewed. The raw surface healed over readily, and

in July there was only one suspiciously red, slightly elevated nodule. Four months later this ulcerated, and then formed a crust, which fell and was renewed from time to time, but in May, 1904, it was still only one-eighth of an inch in diameter. Above it was a group of small, pearly, non-ulcerated nodules. Three exposures produced only a slight redness, but removed both lesions, except for a very thin crust on the lower. Even this crust disappeared within a month, and on September 19, 1904, the skin was perfectly smooth and soft, and showed no trace of a recurrence.

CASE III.—Male, aged fifty-nine years. In February, 1903, the patient first noticed a small, firm nodule in the left lower eyelid, near the border. It gradually increased in size and ulcerated, but without pain. On September 12, 1903, there was an ulcer about a quarter of an inch long by an eighth of an inch broad with a clean, moist base, and a firm, raised, perpendicular border. *x*-ray treatment was then begun, and by November 10 the ulcer was entirely healed. On December 9 a small, pearly nodule was visible, about a quarter of an inch external to the old scar, and the treatment was resumed, and continued with biweekly intervals up to January 28, 1904, when the induration was scarcely perceptible. The patient wrote on September 16, 1904, that there was then no trouble at the eye.

CASE IV.—Male, aged seventy-six years. The patient noticed several scaly patches on the face for about four years, and for the last six months a spot on the right malar eminence, on which a crust formed from time to time, occasionally falling and leaving a lightly bleeding surface. This lesion gradually extended upward, leaving a clear surface below, and at the beginning of treatment, March 20, 1904, was three-quarters of an inch in diameter, and covered with an adherent crust. There was no abnormal sensation save itching. One exposure of eight minutes was given, the anode being three and one-half inches from the skin. On May 9 the lesion had entirely disappeared, leaving a smooth, slightly red surface. The patient reported by letter, September 8, 1904, that the cheek was then well.

CASE V.—Male, aged sixty-one years. A pimple appeared on the left side of the patient's nose about 1895, and gradually spread into a broad superficial crusted patch. It was diagnosed as lupus erythematosus, and treated with local applications, with but slight improvement. Many flat seborrhœal warts developed on the face and hands, and in March, 1902, one of these, on the left malar eminence, became distinctly epitheliomatous. It advanced steadily until in October it had become a deep ulcer about three-quarters of an inch in diameter, with hard raised edges. Between October 21 and December 1, 1902, it was exposed to the *x*-rays sixteen times, aggregating ninety-seven minutes. This produced a moist dermatitis, which subsided in about three weeks, in which time

the ulcer was replaced by a smooth soft scar. The patient had occasional x-ray treatments later, but very irregularly. When last seen, on December 23, 1903, there was no trace of a recurrence of the epithelioma, and the area which had been inflamed by the active treatment was free from warts, while on the rest of the face these were quite numerous, though they always improved temporarily under mild x-ray treatment. The patient's niece wrote, September 12, 1904, that his face was well, except for a small spot on his nose and a very small place on his right cheek, which are presumably part of the old warty condition.

CASE VI.—Female, aged seventy-six years. For two or three years the patient had a small crusted spot about an inch below the left eye. She picked off the crust from time to time, but in September, 1902, it became adherent and bled a little when rubbed. There was a little itching occasionally, but no other sensation. Then for about a year she tried various mild ointments, but without improvement, and when the x-ray treatment was begun there was a hard, elevated, crescentic border about one-eighth of an inch wide and three-eighths of an inch long, with a shallow ulcer below it. Between September 18 and October 20, 1903, it received eight x-ray exposures, aggregating forty-three minutes. This made the skin very red and tender and produced some scaling, but the dermatitis subsided quickly, and by November 28 the skin appeared normal. On September 8, 1904, her son reported that there was still no sign of return, and that the scar was scarcely visible.

CASE VII.—Male, aged forty years. In his boyhood the patient had a boil on each cheek, which on healing left scars. That on the left cheek is now small, depressed, and white. That on the right began to change in 1889, forming a thin scale which gradually increased, then fell, and formed again. The lesion was scraped in 1891, and later was several times burned with acids and with the cautery, but it always recurred and spread. In October, 1902, there was a scar on the right cheek, bounded by a line extending from just below the inner canthus to the sulcus nasi, thence outward about an inch, upward to a spot about one-half an inch below and external to the outer canthus, and thence inward about a quarter of an inch below the free border of the lower lid to the point of origin. The border was elevated and dotted with firm, pearly nodules, which were most prominent along the upper border; similar nodules occurred in the scar itself. At the sulcus nasi was a depression about one-eighth of an inch deep, with hard borders. He received thirty exposures, aggregating three hours and fourteen minutes, between October 16, 1902, and January 2, 1903, when he stopped treatment on account of business affairs. There was a moist dermatitis over the lower part of the scar in November, but no more than a slight redness at any other time. At the time of the last treatment there was scarcely a trace of the disease—only

a little elevation along the outer and upper borders. In March, the area was entirely healed, and no nodules were visible, but in August, 1903, a nodule appeared in the right sulcus nasi. This twice broke down and healed again, hardly changing its size, and in September, 1904, the patient writes, it was still a small, firm, white nodule. The rest of the scar was normal.

CASE VIII.—Female, aged eighty-one years. In the summer of 1902 a small spot like a black-head appeared in the left labio-nasal fold. It grew very slowly for about six months, and then formed a scab, which fell, to be replaced by another, and this process continued, with gradual increase in the size and hardness of the lesion. On September 10, 1903, there was a thin, hard mass about one-half an inch across in the skin of the upper lip close to the left ala nasi. It was depressed in the centre, where the epithelium was wanting, and surrounded by a narrow red zone. Between September 10 and October 19 the spot received eleven exposures, aggregating fifty-nine minutes. The reaction never went beyond a slight redness. On October 29 the lesion was replaced by a pale, slightly depressed scar, which steadily became less conspicuous. At her last visit, June 1, 1904, the scar showed no sign of recurrence, and she wrote September 3, 1904, that it was still perfectly well.

CASE IX.—Female, aged seventy-five years. The patient first noticed a greasy, warty growth on the left side of the nose early in 1902. It grew worse in spite of local treatment, and by September 1, 1903, it was distinctly epitheliomatous. Between September 1 and September 16 the spot was exposed to the *x-ray* seven times, aggregating twenty-nine minutes. The patient then left the city. The lesion showed no change in that time, save an increase in redness, but it healed entirely during October, and the patient wrote, September 10, 1904, that it was still well, while a smaller patch on the nose, which she had declined to submit to *x-ray* treatment, remained, and was slightly inflamed at times.

CASE X.—Female, aged sixty-four years. In 1895 a small tumor appeared on the right side of the upper lip, about a quarter of an inch above the vermilion border. Between December, 1898, and January, 1902, it was scraped six times, and was treated with various ointments, but it always recurred, the last time in June, 1902. The growth was very slow, however, and in June, 1903, there was only a single pearly nodule, barely one-eighth of an inch in diameter, on the border of the small scar left by the previous curettings. Between June 20 and July 15 it received eight *x-ray* treatments, aggregating thirty-five minutes, and producing a mild dermatitis, which subsided quickly, leaving the skin perfectly smooth. The patient wrote September 5, 1904, that there was still no recurrence.

CASE XI.—Male, aged forty-one years. The disease began in January, 1901, as a cold sore. This was irritated by biting, and increased in size in spite of various local applications. On July 1,

1903, there was a hard, thick, slightly elevated mass about five-eighths of an inch in diameter, slightly eroded in places, and situated just to the left of the middle of the lower lip. It was exposed to the x-ray about every second day for two weeks in July, and again for two weeks in August, with slight improvement. The treatment was given also for five consecutive days in October, and for the four days ending December 25, 1903. The last two courses were much more severe than the first two, and were each followed by a considerable inflammatory reaction. This soon subsided, however, leaving the lip apparently normal. On August 17, 1904, the lip showed no induration whatever, only a faint scar, a little light in color at the border, but without nodules.

CASE XII.—Male, aged sixty-five years. The patient was a heavy smoker for many years, using a clay pipe. In the summer of 1902 he noticed a scab on the middle of the lower lip, and picked it off, but it formed again. After that the scab always returned after removal and the diseased area gradually increased in size, until in October, 1902, it formed a circular ulcer about three-eighths of an inch in diameter, with a pale, moist base, and firm, elevated and slightly everted border. The mass was tender only on the skin edge. It was exposed to the x-ray nearly every day from October 9 to November 8, with very little change. Between November 8 and November 19 the original tumor and an enlarged lymph node under the chin were removed at the City Hospital. A second operation was performed about June 21, 1903, for a recurrence in the glands under the chin, and the patient died three days later—of pneumonia, I was told.

CASE XIII.—Female, aged fifty-five years. About 1889 a wart-like spot appeared on the left side of the patient's nose. She picked it and it gradually developed a scab. About a year later it disappeared under mild applications, but recurred, and from that time on it was repeatedly scraped and cauterized, always recurring, and healing in one place only to advance in another. In October, 1902, the middle of the dorsum and left side of the nose were covered with a thin scar, while on the left cheek, about half an inch below the inner canthus, was a hard lump in the deeper layers of the skin, about a quarter of an inch in diameter, in whose lower quadrant was a shallow ulcer, extending also into the sound skin below. x-ray treatment was begun October 8, 1902, and was pursued faithfully. The ulcer soon healed, but the mass above it, while it diminished at first, did not disappear, although the exposures were pushed repeatedly to the production of a dusky redness, and even of a little exudation. The improvement was so slight that operation was advised, and the nodule was removed under ether September 22, 1903. The operation wound broke down in about a week, leaving a small, rather deep ulcer with infiltrated borders. x-ray treatment was resumed at once, and the ulcer healed quickly. As

before, the hardness was more resistant, but by August, 1904, it had nearly disappeared. The repeated exposures, however, had made the skin very tough and palpation was difficult.

CASE XIV.—Male, aged seventy-nine years. About 1901 a scab appeared in front of the right ear. This gradually spread and the skin beneath became indurated, and finally ulcerated. At first the growth was very slow, but for the last two or three months it was much more rapid. During this time the ulcer was treated with silver nitrate in solution, with mercurial ointments, and with hydrogen peroxide, which inflamed it greatly. April 4, 1904, there was an ulcer about one-quarter of an inch broad and three-quarters of an inch long, and surrounded by a red border one-eighth of an inch wide, immediately in front of the right ear. A little pus and serum exuded from the lower part of the ulcer. The tissue beneath was very firm and tense, and it was impossible to tell how much of the infiltration was inflammatory and how much was new-growth. Between April 4 and May 16 it received fourteen  $x$ -ray exposures, aggregating forty-six minutes. The ulcer had healed over by this time, and the mass was less hard, though considerable induration still remained. The patient then went abroad. He called again September 15, 1904, and reported that within two or three weeks of the last visit the skin seemed well and that he had no abnormal sensation. At present there is a single small pearly nodule at the site of the old lesion. But deep in the skin and in the subcutaneous tissue the old hard mass still remains, almost unchanged since May.  $x$ -ray treatment has been resumed and will be continued vigorously.

CASE XV.—Male, aged seventy-one years. Early in 1902 a small papule, covered with a crust, formed on the patient's left cheek near the nose. It spread gradually, and late in the year, after  $x$ -ray treatment by another physician, became inflamed. When first seen in January, 1903, it formed a protuberant mass about three-quarters of an inch long and half an inch broad, very red, and moist in places. Under mild ointments the inflammation subsided, leaving only a slight induration. A single  $x$ -ray treatment was given in April. The patient did not return until September, when the induration had spread and the skin had ulcerated. Again the ulcer healed under the  $x$ -ray, and the induration diminished, and again the patient disappeared for five months, returning in April, 1904, with a hard mass three-quarters of an inch long by one inch wide, situated in and beneath the skin about three-quarters of an inch below the left eye. The upper part was about a quarter of an inch thick—the lower part thinner, and the whole slightly movable on the bone. The  $x$ -ray treatment was resumed and the reaction carried twice to a marked dermatitis, resulting in a diminution in the size of the growth, when again the patient disappeared. He returned in September, 1904, the tumor having increased in size and hardness, and having again ulcerated in the middle.



CASE XVI.—Male, aged sixty-six years. The patient noticed for eight or ten years a wart-like growth on the right ala of the nose. It varied in size, but was never larger than a split pea. Two or three months before applying for treatment he noticed a scab forming on this wart; it fell from time to time, but always was renewed, and during the last six weeks there was a persistent and growing ulcer. When first seen, in April, 1903, there was an irregular ulcer about one-eighth by three-eighths of an inch, on the right ala of the nose, with an indurated border, and a pale, uneven base exuding a slight serous discharge. The induration extended beyond the border. Between April 8 and May 6, 1903, the ulcer received eight treatments, aggregating forty minutes. In this time the ulcer healed but an indurated pearly area remained, and a month later there was a patch of firm epitheliomatous tissue about one-sixteenth of an inch broad by one-half an inch long, with two narrow cracks covered with brownish scales. But the patient considered himself cured, and stopped treatment. I have not seen him since, but he writes, September 10, 1904, that there was little change until last winter, when the disease grew worse, and again improved under *x-ray* treatment. This summer, for the third time, the growth increased its activity, and is now under *x-ray* treatment.

CASE XVII.—Female, aged forty-one years. The growth appeared in November, 1902, as a yellowish papule with a black centre, on the right side of the nose. It was irritated by pricking, and gradually increased in size. It was curetted January 12, 1903, but very incompletely, and then it grew more rapidly than ever, forming, on January 22, an ulcer a quarter of an inch broad and half an inch long, with a hard, raised edge, sloping sides, and a dry, yellowish base, surrounded by a narrow zone of inflammation. Between January 22 and March 2 it received twelve *x-ray* treatments, aggregating one hour and sixteen minutes. The ulcer had diminished one-half, and the edge had grown much softer. The patient called but once again, April 16, 1903, when an exposure of ten minutes was given, and she has not been heard from since.

CASE XVIII.—Male, aged eighty-six years. A little over two years before applying for treatment the patient noticed on the left temple a little indentation covered with a crust, and ascribed it to a razor cut. The crust alternately formed and fell, the lesion steadily growing until January 17, 1903, when it was half an inch in diameter, with a raised, pearly, indurated border and a red, scaly, slightly depressed base, which bled easily. It responded readily to *x-ray* treatment, and had nearly disappeared, when on March 30, 1903, the patient died from the rupture of an artery, after an illness of eight hours.

No.	Age	Site.	Duration before treatment.	Period of treatment.	Result.
1	41	Temple.	12 years	2½ mos.	No recurrence after 1 year and 5 months.
2	78	Front of ear	2 "	1 yr. 7 mo.	" " " 4 months.
3	59	Lower eyelid	7 months	5 months	" " " 8 "
4	76	Cheek	6 "	1 day	" " " 5½ "
5	61	"	7 "	6 weeks	" " " 1 year and 9 months.
6	76	"	2-3 years	1 month	" " " 10½ months.
7	40	"	13 "	2½ mos.	Recurred after 7 months.
8	81	Nasolabial fold	1 year	5½ weeks	No recurrence after 10½ months.
9	75	Nose	1½ years	2 "	" " " 1 year.
10	64	Skin of upper lip	8 years	4 "	" " " 1 year and 2 months.
11	41	Lower lip	2½ years	6 months	" " " 8 months.
12	65	" "	2 months	1 month	No improvement; operation. Death after operation for recurrence 6 mos. later.
13	55	Cheek	13 years	1 yr. 10 mo.	Improved; growth never entirely removed.
14	79	Front of ear	3 "	6 weeks	Improved; ceased treatment.
15	71	Cheek	1 year	1 yr. 3 mo.	" " irregular treatment.
16	66	Nose	3 months	1 month	" " ceased treatment.
17	41	"	2 "	5½ weeks	" " "
18	86	Temple.	2 years	2½ mos.	" " death from intercurrent disease.

Of the whole series of 18 cases, 1 (Case XVIII.) died of intercurrent disease and 4 (Cases XIV. to XVII.) were too brief or too irregular in their attendance to get permanent results. Of the remaining 13 cases, in whom the method had a fair trial, 1 case (Case XII.) showed no improvement after one month of treatment; in 1 (Case XIII.) the condition was improved, but the growth never entirely removed; and 1 (Case VII.) was apparently cured, but had a recurrence seven months later. The remaining 10 (77 per cent.) showed no recurrence after periods ranging from four months to one year and nine months.

Case XII., who showed no improvement, had a rapidly growing epithelioma of the lower lip—a type now recognized as being very difficult to heal with the *x*-ray. Still, it is possible that longer and more vigorous exposures might have arrested the growth, as indeed happened in Case XI., and it is very probably that his death was due directly to an inhalation pneumonia dependent on the second operation.

Case XIII., in whom the growth never entirely disappeared, was very similar to cases XIV. and XV., who also were very hard to influence. The distinguishing mark in all three was an almost stony hardness deep in the skin and the subcutaneous tissue, covered in great part or entirely with apparently normal epithelium, and showing very little tendency to ulcerate. The ulcer, if present, heals readily, but the hard mass beneath yields slowly or not at all. They require very intense treatment, and I believe that many of this class cannot be cured by the *x*-ray unless an ulcer is produced.

In marked contrast with this type of epithelioma is that represented by Cases I. to X. and Cases XVI. to XVIII. The common and characteristic mark of this group is the superficiality of the lesion. The induration seems to be in the skin itself, and quite

near the surface—never deep, as in the resistant type. The borders are generally narrow, slightly elevated, firm, grayish-white, and composed either of separate pearly nodules or of such nodules run together to form a ring or part of a ring. The base is sometimes fairly deeply excavated, as in Case V., but usually it is only a little below the level of the surrounding skin. It is sometimes bright red, and moist from exuded serum, but the exudation is never very great, and often dries to a scab, which falls from time to time, or which may be pulled off, leaving a moist, easily bleeding surface; or the base may be only delicate pink scar tissue. In the above series but one case of this type (Case VII.) recurred.

Before closing there is another class to be mentioned, for whom x-ray treatment is invaluable—a class dependent on the patient rather than on the type of disease. It includes that large group of cases in which any radical operation is impossible, is inadvisable, or is refused. Besides the frankly inoperable cases which every surgeon knows, and those whose horror of the knife is such that any cutting operation is out of the question, there are many patients who by reason of age or of bodily infirmity would be placed in much greater danger by an operation than they suffer from their disease. Case II. is a good example. He is a man of seventy-eight years, in good general health, but not strong enough to run the risk of a general anæsthetic. He is now, four months after his last treatment, absolutely free from all signs of recurrence. But even should the growth return there is every reason to believe, from his previous history, that it could at least be held in check, and long before he could suffer any inconvenience from it he will probably die from some intercurrent disease—as actually happened in Case XVIII. For such cases the safety, the convenience, and the painlessness of the method are its great advantages; and to these advantages we may add, if the lesions be superficial, a reasonable hope of permanent cure.

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## A STUDY OF ACUTE HEMORRHAGIC ENCEPHALITIS (STAPHYLOCOCCUS PYOGENES AUREUS).

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FOLLOWING is a study of encephalitis in man, due to the staphylococcus pyogenes aureus. Parallel lesions have been studied in

guinea-pigs, with a view to establishing the time limits and order of the acute inflammatory changes.

A text for the present work was afforded by some points of a case, previously reported at length,<sup>1</sup> of cortical hemorrhages ensuing upon subinfection with the staphylococcus pyogenes aureus during convalescence from scarlet fever in a boy aged five years. An abstract of this case follows:

CASE I.—*Abstract.* About five weeks after onset of scarlet fever, convalescence was interrupted by cerebral symptoms, and death occurred two weeks later (seven weeks after admission). The contractions and sensory symptoms began in the right leg and advanced during four days to affect the whole right side, including the face. The contractions were sharply defined (at one time alternating regularly with relaxations at intervals of about ten seconds) and limited in duration (a few minutes). Paralysis of the affected limbs ensued. During the last week the child was in the main unconscious (masking symptoms on left side).

At autopsy the organs and tissues showed little gross evidence of lesion, beyond desquamation of skin and fresh and pigmented hemorrhagic lesions in the cortex of both parietal lobes, with œdema of overlying pia mater.

Microscopic study showed an early bronchopneumonia and septicæmia (staphylococcus pyogenes aureus) and a purulent inflammation of foci in the parietal pia mater and overlying arachnoidal villi. Besides large areas of hemorrhage in the cortex, there was extensive development of cells phagocytic for polynuclear leukocytes, blood corpuscles, and fatty detritus. These phagocytes lay in meshes of the pia mater and in the adventitia of the short arteries of the cortical system. The phagocytosis was accompanied by solution and fatty changes of adjacent nerve tissues. Fatty changes in associated motor systems and early changes (axonal degeneration of anterior horn cells by Nissl method) in the lower motor systems.

The interpretation of Case I. is not wholly clear. Suspicion, however, attaches to the staphylococcus pyogenes aureus and its toxins for the production of some of the cerebral lesions. A study has therefore been made of further accessible cases of septicæmia and encephalitis associated with the staphylococcus aureus to find what aspects are held in common. Abstracts of these cases follow:

CASE II.—*Clinical History.* A. B., a girl aged twelve years, was admitted to Dr. G. C. Sears' service at the Boston City Hospital January 7, 1901. On entrance she was wildly delirious. Her head was retracted, and there was spasm of the posterior cervical muscles, with inability to flex the head. The pupils were widely dilated and failed to react to light. Both tonsils were enlarged, and the tongue

<sup>1</sup> E. E. Southard and F. R. Sims. A Case of Cortical Hemorrhages following Scarlet Fever, Journal of the American Medical Association, September 17, 1904.

bore a heavy white fur. There was a loud, rough, systolic murmur audible throughout the heart area, but at its maximum in the second left intercostal space and over the apex. The murmur was transmitted into the vessels of the neck, the axilla, and the back. There were a few moist rales at bases of lungs behind. The abdomen was everywhere tympanitic, and there was slight voluntary spasm of the walls. The reflexes were normal. Over outer aspect of right ankle, extending from a point 18 cm. above external malleolus to the heel, was an erythematous swelling, acutely tender and painful on passive motion. Below malleolus were three small pustules with incised (surgical) wound.

The origin of this condition is unknown. Four days before she had the first symptoms of her illness, chilly feelings and frontal headache. The next day small black spots were noted on the right foot, and an incision was made. The next day (third of the attack) she vomited after meals. Then gradually supervened the condition at entrance as above described.

The girl was fairly well developed, but poorly nourished. She is said to have had rheumatic fever at six years of age, scarlet fever at nine, measles at ten, and was just recovered (five weeks) from diphtheria. It is not possible to say what importance attaches to any of these events.

The day after entrance fresh inflammatory areas developed over the head of the fifth metatarsal bone of the left foot and the inner aspect of the left wrist. The leukocytes were but 10,000 per c.mm. The patient immediately vomited the food administered by nasal catheter.

The evening of the third day after entrance the patient died without notable change of condition.

*Clinical Summary.* Girl, aged twelve years, just recovered from diphtheria, with history of rheumatic fever, scarlet fever, and measles. Onset of attack, chilly feelings, and frontal headache, with development of purulent hemorrhagic areas on right foot, and vomiting two days later. Four days after onset, admitted in delirium, with suppurating wound of heel and heart murmur. Retraction of head. Dilatation of pupils, which failed to react to light. Development of fresh superficial inflammatory areas. Death eight days after onset of symptoms.

The autopsy was performed by one of us (E. E. S.) January 10, 1901. Following are the findings in the head:

Brain, weight 1200 gms. Dura tense, convolutions somewhat flattened. Density of brain about normal except right occipital lobe, which is semifluctuant. On section there is found near the apex of this lobe a rather firm, irregular mass of clotted blood, 3 cm. in greatest diameter. It reaches to within 1 cm. of surfaces of brain, but does not show externally. Around the clot is more or less fluid blood. The adjoining brain tissue for some distance is

stained reddish-brown and is of soft consistence. The hemorrhage has extended into the right lateral ventricle, where fluid blood is present. A little is present also in the left ventricle.

*Anatomical Summary.* Wound of heel, with purulent infiltration of adjoining tissues; infective thrombus left ventricle wall; multiple abscesses of heart wall, kidney, adrenal, liver, spleen, intestines; diffuse small hemorrhages of lungs, kidney, epicardium; hemorrhages and softening of right occipital lobe; fatty degeneration of myocardium and skeletal muscles; chronic endocarditis (mitral); chronic adhesive pericarditis; chronic pleuritis of left lung and right apex.

*Microscopic Findings.* Cultures from the organs showed a septicæmia due to the staphylococcus pyogenes aureus. The growths were pure except from the kidney, which showed, besides the staphylococcus, an organism of the colon-typhoid group.

The histological examination of the various organs confirmed the diagnoses from gross findings. The lung shows small hemorrhages, chiefly without leukocyte reaction. The marrow of the femur is very cellular, containing numerous leukocytes of the mononuclear series, but very rare polynuclear leukocytes.

Special study of tissues from the brain was made by a variety of methods.

The subcortical lesion in the occipital lobe shows wide sheets of clear, well-preserved blood, with occasional polynuclear leukocytes and several foci of staphylococci, both free and within cells. The hemorrhage penetrates the cortical tissue along lines of least resistance between the radiating bundles of nerve fibres. Occasionally large vessels from the cortical system run free through the blood, with the adventitial meshes dilated with polynuclear leukocytes and occasionally embraced by areas of coarse fibrin. Near the vessels there occur purulent areas, with fatty changes, pigment, fat-containing and pigment-containing phagocytes, and without notable evidence of repair. Adjacent to the hemorrhagic areas the myelin, as a rule, stains perfectly; but a few fibres are represented in Marchi sections by linear collections of black dots. The nerve cells occasionally show changes, as a rule attributable to swelling or shrinkage due to œdema. These changes are scarcely more marked near the hemorrhage than remote from it.

CASE III.—*Clinical History.* H. H., a man, aged twenty-two years, was admitted to Dr. G. B. Shattuck's service at the Boston City Hospital, December 5, 1903. On entrance he was unconscious and restless, with flushed cheeks and equal, contracted pupils, reacting sluggishly to light. There was slight rigidity and retraction of neck. The abdomen was slightly retracted and rigid, with tenderness over pubes. The legs were flexed and rigid. The hands and feet were blue, and there were irregular hemorrhagic areas about thumbs and over outer surfaces of both feet and the toes.

The knee-jerks were normal. Kernig's sign and Babinski's sign were absent.

The attack had begun the day before, with increase in frequency of micturition and general discomfort. The physician, Dr. C. L. Knight, had forthwith suspected cystitis, as he had had the patient under treatment for some time for urethritis. In the afternoon of the day before admission the patient complained of severe pains in various parts of the body, especially the thumb and ankle. Nausea, vomiting, and delirium followed.

The day after admission (the third day of the symptoms) the patient died, without marked change of condition. The pulse, at first of moderate rate, later became rapid, small, and easily compressible. Cyanosis increased. The chest became filled with moist rales. The ecchymoses of the extremities slowly increased in extent. The pupils became widely dilated and still reacted sluggishly to light. The reflexes remained as before; there was some question whether Babinski's sign was present.

*Clinical Summary.* Man, aged twenty-two years, with history of treatment for urethritis. Onset of attack with increased frequency in micturition and malaise. Later in the day various focal pains, nausea, vomiting, delirium; cyanosis; ecchymoses on thumb, ankles, and toes. Pupils at first contracted, before death dilated. Death on the third day.

*Autopsy Findings.* The autopsy was performed by Dr. R. L. Thompson and one of us (E. E. S.) December 7, 1903. The findings in the head were:

*Head.* Hair dark and fairly thick. Scalp normal. Cranium of the usual thickness. Dura externally smooth and tense. Sinuses contain fluid blood with cruor clot. Pia over left hemisphere almost dry, and tightly stretched over flattened convolutions and effaced sulci. There are a number of irregularly distributed ecchymoses, varying in diameter from a pin's head to 0.5 cm. or more, rarely 0.75 cm., either within meshes of pia at lips of sulci or shining through from cortical substance. In the region of the left supra-angular gyrus are two well-defined ecchymoses, with irregular and re-entrant borders (0.5 cm. and 0.75 cm. in diameter, respectively), containing in the middle pinhead foci of frank, yellowish-green pus. The pus has not broken through the pia. Pia over right hemisphere contains a slight amount of clear fluid, but is externally almost dry. Effacement of sulci by pressure has just begun. Pia on both sides shows a well-marked injection, with minute, tree-like tracery in the superficial cerebral venules. About some ecchymoses are delicate pink areas of diffused blood pigment (some of which may be of post-mortem origin). Vessels at base normal.

*Cerebrum.* The core of the left occipital lobe is replaced with a walnut-sized mass of loosely clotted blood, resting in a bed of moist, grumous, pinkish-gray detritus. Beyond the zone of dis-

integration is œdematous white matter, with distinct puncta cruenta and minute hemorrhages. The cortex of the occipital pole is destroyed, and the hemorrhage points also upon the posterior horn of the left lateral ventricle, into which has oozed several cubic centimetres of blood, now clotted *in situ*, with a little staining of posterior portion of choroid plexus. There is no gross evidence of old abscess or other lesion than hemorrhage in this area. It is probable that the hemorrhage is from a medullary branch or branches of the cortical arterial system.

The core of the right occipital pole shows a similar area of hemorrhage (from the medullary branch of the cortical arterial system), thimble-shaped, giving destruction chiefly of white substance with a small portion of cortex. The pia is just tangent to the lesion, which is, therefore, scarcely evident from without.

The substance elsewhere is slightly moister than usual, and both cortex and white matter contain fairly numerous, pinhead, purplish areas of hemorrhage, without evidence of pus. These areas are somewhat more frequent on left side. The substance on section shows a slight retraction of white matter (or release of tension in gray?) and a diffuse appearance somewhat suggestive of encephalitis, but there is no relatively normal white substance with which to compare.

The basal ganglia and lower system are spared from lesion. There are a few ecchymoses in the cerebellum.

*Brain.* Weight 1265 gms.

*Anatomical Summary.* Acute endocarditis; acute pericarditis; multiple abscesses of liver, kidney, and thyroid; infarcts of small intestine; acute splenitis; hyperplasia of mesenteric lymph nodes; acute fibrinous pleuritis (left); œdema and congestion of lungs; acute purulent bronchitis; interstitial orchitis; œdema and congestion of brain; multiple ecchymoses of white and gray matter; abscesses of cortex; hemorrhages into occipital poles (probably from medullary branches of cortical arterial system).

*Microscopic Findings.* Cultures from heart's blood, pericardium, mitral valve, liver, spleen, kidney, right centrum semiovale, left occipital lobe, and abscess on heel showed staphylococcus pyogenes aureus.

Histological examination of the organs of the trunk showed in the main the lesions diagnosed from gross appearances. The kidney shows a focal chronic interstitial process.

In the subcortical regions of certain foci in the cerebrum and the cerebellum are well-defined abscesses of a characteristic type. A central colony of staphylococci is surrounded by polynuclear leukocytes in a zone, which is in turn surrounded by a zone of fresh hemorrhage. These areas are sometimes a millimetre in diameter, but are, as a rule, merely punctiform. Beyond the lesions there is usually no sign of tissue reaction.



CASE IV.—*Clinical History.* M. M., a woman aged forty-two years, was admitted to Dr. G. C. Sears' service at the Boston City Hospital March 14, 1902. On entrance she was mildly delirious. There was well-marked sclerosis of all palpable arteries, and the heart showed at the apex short systolic and presystolic murmurs, heard also in axilla and back; a systolic murmur was audible at base and in aortic and pulmonary areas. The right lung was dull below the fifth rib in the axillary line (respiration and vocal resonance distant, tactile fremitus diminished). There were friction sounds opposite the right fifth rib. The left base showed many moist rales. Abdomen, dull in flanks, showed fluid wave. There was considerable oedema of ankles and legs. The pupils were equal and reacted normally.

The woman is said to have had influenza three years before, after which she had suffered from dyspnoea, palpitation, and frequent micturition. The menopause had occurred three months before onset of present illness. For four months she had had a slight cough. A week before entrance she had taken to bed with a sharp attack of pain in the right chest, followed by rapid and progressive increase in dyspnoea and increase of cough, with frothy expectoration.

After admission her condition grew worse; she became noisy and garrulous and required restraint. A week after admission she got out of bed during the night and injured her right eye. The upper lid had to be incised some days later, and two drachms of pus were evacuated. Constipation set in, with palpable fecal masses over abdomen. The orbital suppuration grew gradually better, but on the twenty-third day after admission (two weeks after injury to eye) an erysipelas-like condition developed about the eye. Thenceforward the patient gradually failed, and a week later died.

*Clinical Summary.* Woman, aged forty-two years, just after menopause, with arterial and cardiac sclerosis. Pleurisy with effusion, gradually deepening delirium, injury to eye with suppuration (a week after admission, two weeks after onset of pleurisy), and constipation. Death three weeks after injury to eye, a week after development of erysipelas-like condition about eye, two days less than a month after admission.

*Autopsy Findings.* The autopsy was performed by Dr. W. R. Brinckerhoff April 14, 1902. The findings in the head were:

*Brain.* Weight, 1270 gms. Dura and sinuses normal.

*Middle Ears.* Normal.

On the external aspect of the right temporal lobe is a small abscess (3 mm.) surrounded by a zone of injection. Similar smaller abscesses are present over the vertex. On section, ventricles contain considerable amount of clear, straw-colored fluid. The substance of the cerebrum appears normal. Cerebellum normal. In the middle of pons is a circular area 6 mm. in diameter, which is some-

what soft and of a black color. This area is sharply circumscribed. Its greatest diameter is lateral, not appearing in the adjacent sections 5 mm. apart. The surrounding brain substance appears normal.

*Anatomical Summary.* Pleurisy with effusion (right side); hydropericardium; multiple abscesses of heart, kidneys, spleen, lung, and brain; ulcerative colitis and proctitis; chronic diffuse nephritis; acute cystitis; uterine fibromyoma; general arteriosclerosis; chronic splenitis; small hemorrhage in pons.

*Microscopic Findings.* Cultures from liver, spleen, and kidney showed pure growths of staphylococcus pyogenes aureus. Histological examination of the various organs confirmed the diagnosis of septicæmia. No cultures were taken from the brain abscesses, which were saved entire for histological purposes; but there can be no doubt of the relation of the staphylococcus to the abscesses. The special points in the histology of this case are brought out in the following:

The lesions beneath the pia mater of the temporal lobe, for example, consist of a central colony of staphylococci in and about a vessel which is surrounded by a zone of polynuclear leukocytes, often phagocytic for the bacteria. Among the polynuclear leukocytes are numerous larger phagocytes, now of the compound granule type, elsewhere containing chromatic material derived, as a rule, from polynuclear leukocytes. The large phagocytes sometimes contain bacteria as well as remains of tissue cells. Outside the zone of polynuclear leukocytes is a broader zone, consisting almost purely of cells of the phagocyte group, here in most instances of the compound granule type. Beyond these zones of nucleated cells is a zone of pure and well-preserved blood. There is nowhere any notable amount of fibrin. There are in many places small vessels plugged with staphylococci, some of which have grown post-mortem.

The sections from the pontine lesion are of note by reason of the juxtaposition of the fresh hemorrhagic lesions with an older cystic lesion. The older lesion consists of a small cavity, about 2 mm. in diameter, lined by a condensed layer of neuroglia and filled with large, vacuolated phagocytes and granular material. The neuroglia lining is interrupted in places by slender projections due to vessels invested by a thin layer of oval, fibrillated glia cells. The fresh lesions show blood free in the meshes of the tissue, with here and there a large phagocyte and polynuclear leukocyte and without notable amounts of fibrin. The surrounding tissue shows no reaction beyond an increase in the volume of the cell bodies in some neuroglia cells.

CASE V.—*Clinical History.* J. C., blacksmith, of middle age, was admitted to Dr. A. L. Mason's service at the Boston City Hospital December 3, 1897. He was brought to the hospital

delirious and unconscious in an ambulance, having fallen in the street.

Physical examination showed the left pupil slightly larger than the right, knee-jerks absent, pulse feeble but regular, chest slightly hyperresonant, pleural rubs in left axilla and lower back, and a temperature of 104°. The urine showed 0.5 per cent. albumin. The patient died the day after admission without change of condition.

*Autopsy Findings.* The autopsy was performed by Dr. F. B. Mallory December 4, 1897. The findings in the head were:

*Brain.* On the right side of the pia 3 cm. from the median fissure, and in the sulcus just back of the fissure of Rolando, were three, minute, yellowish specks, apparently miliary abscesses. The surrounding brain tissue was œdematous and swollen and the pia contained minute hemorrhages. In the substance of the brain no lesions could be found anywhere.

*Middle ears* normal.

Sinuses of nose and the antrum of Highmore on each side were all normal.

*Anatomical Summary.* Septic infarctions of lungs; metastatic abscesses of kidneys and meninges; acute fibrinous pleurisy; chronic adhesive pleurisy; congestion of lungs.

*Microscopic Findings.* Cultures from organs of the trunk showed pure growths of the staphylococcus pyogenes aureus, except that from the kidney, which showed also an organism of the colon-typhoid group.

Histological examination confirmed the diagnosis made from gross appearances. The liver shows some cellular infiltration of the portal spaces and central congestion.

The histological picture presented by the brain varies from a simple meningitis to a diffuse meningoencephalitis. The simple meningeal inflammation consists of an exudate of polynuclear leukocytes, more thickly into the proximal meshes of the pia mater. There is strikingly little blood and a small amount of fibrin in this lesion. There are fewer meningeal phagocytes than usual; but a few lymphatic clefts are filled with such cells containing fragmented polynuclear leukocytes. The exudate follows the cortical arteries into the brain substance in some cases as far as the white matter. The subpial neuroglia and the pyramidal cell layers are for long distances dotted with polynuclear leukocytes of fairly even distribution. It is unusual to find polynuclear leukocytes in apposition with nerve cells. The nerve cells are slightly swollen. The bodies of the neuroglia cells are, as a rule, invisible; but some of the cells of the subpial layer approach the astrocyte in type.

CASE VI.—*Clinical History.* A. M., an Irish woman aged thirty-three years, was admitted to Dr. J. N. Coolidge's service at the Boston City Hospital June 15, 1904. On entrance she was

delirious, half-conscious, and unable to answer questions. There was convergent strabismus and a choreiform or athetoid tendency to co-ordinate movements of both arms. Nothing further was discovered in the physical examination to throw light on the condition. The present illness was said to have lasted ten days, setting in with vomiting, which continued for five days. The strabismus was developing meanwhile, and the twitchings became well marked. She was sleepless and complained of soreness in the abdomen. For years she had been addicted to the use of alcohol, often to excess. The patient died five days after entrance. The choreiform movements persisted until death. The convergent strabismus became more marked. Stiffness of neck developed. The reflexes remained normal.

*Clinical Summary.* Woman, aged thirty-three years, with history of abuse of alcohol, died in delirium fifteen days after onset of an attack of choreiform character, with convergent strabismus, insomnia, and normal reflexes. Onset with vomiting, lasting five days.

*Autopsy Findings.* The autopsy was performed by Dr. S. B. Wolbach June 21, 1904. The description of the head by one of us (E. F. S.) follows:

*Head.* Scalp normal; skull symmetrical; frontal suture effaced. Superciliary ridges and frontal eminences ill-defined. Calvarium opaque by transmitted light and everywhere moderately thickened. The thickening affects chiefly the inner table, and is least marked at the bregma, where the internal surface presents a shallow, diamond-shaped depression corresponding to the anterior fontanelle. The frontal bone shows marked symmetrical thickening, which transforms inner arc to an oblique flat surface, on which there is a slight groove for the superior longitudinal sinus and a few narrow depressions for the meningeal vessels. At a point 4 cm. from the orbit the bone is 1.5 to 2 cm. thick. The diploë is nowhere well marked. The frontal bone is ivory-like on section and of the consistence of the petrous bone. Dura normal. The dura beneath frontal bone is readily separable from the inner table. Sinuses and meningeal veins contain fluid blood. Pial vessels everywhere injected. Arachnoidal villi well developed. Pia of vertex cedematous. Substance moist. Everywhere elastic except in an ill-defined area, including second right temporal convolution. The cortex and underlying white of this region are plastic and readily crushed; the puncta cruenta of the white matter are distinct, and there are a few minute, perivascular hemorrhages. Co-ordinate areas in the left hemisphere are equally moist; but the gray matter does not bulge from the plane of section. The rest of the centrum semiovale shows no more than oedema.

The frontal convolutions are fairly symmetrical. There is no microgyria and no narrowing of gray matter, but there is a slight

increase of consistence in the frontal gyri on comparison with, for instance, the occipital gyri. The frontal and especially the prefrontal region as a whole may be looked on as undersized. Rest of encephalon and spinal cord show less œdema than the hemisphere and no further gross lesion.

*Middle ears* normal.

*Anatomical Summary.* Œdema and congestion of lungs; chronic fibrous pleuritis (left); œdema of pia; cerebral œdema; focal softening of right second temporal convolution (encephalitis); frontal lobes undeveloped; thickening of cranium (most marked in frontal bone).

*Microscopic Findings.* Cultures from organs of the trunk remained sterile. Culture from the white matter beneath the second right temporal convolution showed staphylococcus pyogenes aureus, together with a few colonies of similar appearance which never assumed a golden-yellow color (staphylococcus pyogenes albus?). A culture of the staphylococcus pyogenes aureus derived from this case was used in a portion of the inoculations described below.

Examination of the organs of the trunk showed nothing adequate to account for the history of the case. The lung shows a few *Herzfehlerzellen* in some alveoli and a few bronchi plugged with polynuclear leukocytes in good preservation and without bacterial inclusions. The spleen shows an unusually high percentage of polynuclear leukocytes and fairly numerous eosinophilic leukocytes in the pulp, but is otherwise not remarkable. The liver is slightly fatty; some of the cells central in the lobules are lace-like. The kidney shows a few slender casts in the tubules of the pyramids. Otherwise both the organs mentioned and the others examined show little that is noteworthy.

Co-ordinate places in the hemispheres were examined to detect the extent and nature of the inflammatory process suggested by the gross appearances and the bacterial findings. The two sides are distinguished by the fact that, in the section taken from the cortex and white matter of the right temporal lobe, there are numerous small collections of blood globules, with a few polynuclear leukocytes lying in the meshes of the arterial adventitia. There seldom occur, however, hemorrhages of any great volume. Blood rarely occurs free in the tissue. On comparison with tissue from the opposite hemisphere it is found that very many more distended capillaries have become visible in the cortex and notably in the subcortical region of the right temporal lobe. Several of these capillaries are found packed with polynuclear leukocytes. The neuroglia shows no pertinent differences on the two sides; the subpial glia of the left hemisphere appears denser in structure than in the right in the places examined. Numerous nerve cells are contracted and somewhat densely staining by several of the technical methods employed (eosin and methylene blue, aniline blue con-

nective tissue, and phosphotungstic-hæmatein methods, for example). These cells are possibly more numerous in the left hemisphere than in the right in the places examined. These latter changes are certainly not beyond the range of artefact and are scarcely entitled to specific importance on account of the omnipresent œdema. Yet these cells recall the cells found in certain foci of our experimental material. The cerebellum and the rest of the nervous system as far as examined showed no noteworthy lesion. A few capillaries in the choroid plexus contain numerous polynuclear leukocytes; there is a much smaller number outside the capillaries and none beyond the ependyma.

GENERAL CLINICAL SUMMARY. From the histories detailed above the following *résumé* has been drawn:

Three of the patients were male, three female. Their ages varied from five to fifty-five years.

In every case, excepting Case V., whose past is unknown, there is a history of antecedent disease; thus Case I. was convalescing from scarlet fever; Case II. was five weeks recovered from diphtheria and had a chronic endocarditis of long standing; Case III. was under treatment for chronic urethritis; Case IV. had pleurisy with effusion and was but three months beyond the menopause, and Case VI. had a history of excess in alcohol of many years' duration.

The onset was in three cases sudden (hemiparesis and unilateral convulsions in Case I.; chilly feelings and frontal headache followed by ecchymoses in Case II.; malaise, manifold pains, ecchymoses, and cerebral symptoms in Case III.). Case V., in which the onset is unknown, was in all ways fulminant. In Case IV. the symptoms gradually supervened upon the pleurisy and the orbital suppuration. Case VI. showed a gradual onset.

The syndromes as a whole were of pronouncedly cerebral type in Cases I. and VI., of meningitic trend in Cases II. and III., of septicæmic character in Case IV. Septicæmia could be suspected in all three cases (II., III., IV.) in which superficial ecchymoses or suppuration became prominent.

The temperature varied for the various cases: at times 103° and 104° for cases III. and V.; the temperature in cases II., IV., and VI. was never high and frequently subnormal.

The pulse was in no case subnormal, and, as a rule, ranged above 100. The respirations were, as a rule, increased.

The duration of the encephalitic symptoms cannot in all cases be closely reckoned: Case III., three days; Case IV., one week (after development of erysipelatoid condition) or three weeks (after injury to eye); Case II., eight days; Case I., two weeks; Case VI., fifteen days; Case V., unknown. Thus those cases were of longer duration in which the cerebral syndromes were most clearly marked.

GENERAL ANATOMICAL SUMMARY. Of the gross findings at autopsy the following are to our present purpose: chronic lesions

which might correspond with greater likelihood of bacterial infection were found in several cases; thus, the remains of scarlet fever in Case I., chronic endocarditis in Case II., arteriosclerosis in Case IV.

The phenomena of general infection were found in Cases II., III., IV., and V. Comment is made below upon the correlation of pulmonary lesions with our cases.

The distribution of the brain lesions is as follows:

Four cases (I., II., III., IV.) showed areas of frank and somewhat voluminous hemorrhage, as a rule involving primarily the subcortical region (of the vertex in Case I., of the occipital lobes in Cases II. and III.), and in Case IV. affecting the pons.

Three cases (III., IV., V.) showed multiple ecchymoses and small abscesses of the cortex or subcortical region, with or without gross evidence of surrounding oedema.

In three cases (I., V., VI.) oedema of pia mater was remarked.

In two cases (II. and III.) there was noted an effusion of blood into the lateral ventricles; and in these cases the convolutions were flattened.

In two cases (IV. and VI.) in which the temporal lobe was involved the middle ears showed no lesion. The mucosæ of the head play no such role in this kind of encephalitis as in the massive brain abscesses made familiar by Macewen.

**GENERAL SUMMARY OF MICROSCOPIC FINDINGS.** The staphylococcus pyogenes aureus was found in all cases in culture post-mortem, generally distributed in five cases, in the brain alone in Case VI. The diagnosis of general infection, at least at the time of death, seems warranted in the first five cases. Case VI., in all ways unusual, may possibly be interpreted as showing the first stage of a massive brain abscess; but the middle ear showed no lesion at autopsy. The atria of infection remain obscure in Cases V. and VI. In Cases II., III., and IV. acute endocarditis was found; and, although in none of these cases is the chain of evidence entire, there were present in all three adequate primary lesions (suppurating surgical wound in Case II., chronic urethritis in Case III., colitis in Case IV.).

The microscopic findings in the organs at large call for little comment. Focal pulmonary lesions were either grossly prominent or made out microscopically in all six cases. There was pus in the bronchi of Cases III. and VI., bronchopneumonia in Case I., and there were septic areas of hemorrhage in the lungs of Case II., septic infarction in Case V., and multiple abscesses in Case IV. This coincidence of pulmonary and brain lesions is certainly of clinical importance. A similar coincidence was noted at least as early as the sixties of the last century.<sup>1</sup> Compare also the production described <sup>2</sup>below of meningitis and meningoencephalitis in the

<sup>1</sup> Biermer, Zur Theorie und Anatomie der Bronchienerweiterung, Virchow's Archiv, 1860, xix. S. 244.

guinea-pig by intrapulmonary inoculations. We are not prepared at present to regard this coincidence as a matter of cause and effect.

The microscopic findings in the brains of this series of cases present more features in common than the gross findings. Thus, whereas miliary abscess, punctiform or massive hemorrhage, and ill-defined red softening form quite diverse gross pictures, the microscopic pictures form unitary series or are well-nigh interchangeable.

It is, moreover, by no means scholastic to insist that too close lines cannot be profitably drawn between meningitis and encephalitis. The word "extension" has gained so wide a vogue that one forms the idea that, although a process may extend, the diagnosis somehow should not extend *pari passu*. Meningitis by extension from abscess and encephalitis by extension of pial inflammation are processes of importance, though charged with being merely secondary. It is these secondary phenomena, in especial the encephalitic ones, which, in the cured cases, may afford a basis for our so mysterious scleroses.

The inflammation of meninges and cortical and subcortical substance in man produced by the staphylococcus pyogenes aureus is distinctively hemorrhagic. Very little fibrin is formed in these lesions. The bleeding continues in some cases until stopped by intracranial pressure. Small vessels are, as a rule, affected.

The typical picture is of a central colony of staphylococci in and near a vessel surrounded by zones of polynuclear leukocytes, large phagocytic cells, and blood. Dying nerve cells are sometimes included in the lesion. The neuroglia cells are slightly active about some of the lesions. Fibril production is absent. The myelin sheaths stain well by Weigert to the edge of the lesions, but show fatty changes in Marchi preparations, for a short radius round about. Prominent in these lesions are the fat-containing and leukocyte-containing phagocytes of the type so often found in all kinds of cerebral lesions. The accumulation of these was in no other case so massive as in Case I.; but they are omnipresent. Their frequency and distribution are such that many foci of these lesions look, in accordance with our usual ideas, to be of long standing.

EXPERIMENTAL MATERIAL. As supplement to the histological work on the lesions in man, a series of inoculations of the staphylococcus aureus was made in guinea-pigs and rabbits. Several strains of staphylococci were used, derived from various lesions, including the focus in Case VI. It was found best to employ one species of animal for serial work; and the guinea-pig was chosen. It is easy to include in single sections meninges, substance, and ventricle of the guinea-pig brain. Several methods of inoculation were employed, as beneath the skin, into the lung, through the ear-plate, and beneath the dura. The guinea-pigs stood the inoculations well and,



after recovery from chloroform anæsthesia, as a rule showed no sign of disease up to the time of examination. In some cases they were overwhelmed by the septicæmia. The fatal results are apparently more a matter of individual pig than of culture. The most convenient method was found to be the method by intrapulmonary injection.

By intrapulmonary injection of 0.5+ c.c. of a twenty-four-hour bouillon culture of the staphylococcus of the strains used one is almost certain to produce exudation into the meninges of the guinea-pig. Of this there will probably be no clinical evidence. But examination of the brains of the pigs at suitable intervals will show lesions of fairly rapid evolution. These inoculations have been controlled by subdural inoculations, with examination at similar intervals.

As early as six hours after intrapulmonary inoculation the meninges may show evidence of diapedesis of blood and exudation of polynuclear leukocytes of quite focal character. The ependyma remains clear, and no changes can be detected in the brain substance.

By twelve to fourteen hours after inoculation exudation through the ependyma is likely to be well under way.

Twenty-four hours after inoculation the vessels are injected, and blood and occasional polynuclear leukocytes are likely to be found in the pial meshes. The chief sign of inflammation, however, is the frequent demonstration in the vessels of a row or thin lining of leukocytes in the inert layer.

In one instance after intrapulmonary injection the guinea-pig immediately became paraplegic and was killed after twenty-four hours. The brain showed ependymitis, very marked meningitis, and the most extensive exudation of leukocytes into the brain substance which we were able to procure in the intrapulmonary inoculations. In this case leukocytes were very frequently seen in juxtaposition with the small pyramidal nerve cells. The same phenomenon was found later in the intrapulmonary series (although never so markedly as in this case) and is focally present in several instances in cases of subdural inoculations examined after two or three days. It is perhaps not necessary, in accounting for this occurrence of leukocytes near nerve cells, to invoke a richer lymph system for the guinea-pig brain than for the human brain. Possibly the leukocyte can more easily wander through the substance of the guinea-pig brain because it is less densely fibrillar than that of man.

Forty-eight hours after inoculation, the emigration of leukocytes into the tissue beneath the ependyma is already marked, and numerous examples can be found of leukocytes in apposition with nerve cells.

The cases examined three days after inoculation show meningitis, encephalitis, and ependymitis at their height. The controls by subdural inoculation show far more intense diffuse processes. The

three-day subdural material can be recommended for study of the cells in the lesions produced by this organism.

In material examined four and five days after inoculation the exudate is already altered by the appearance of fairly numerous cells of the lymphocyte series and a number of cells phagocytic for cell detritus.

Six days after inoculation the lesions found are meningitis and pyocephalus, due largely to exudation from the choroid plexuses. The cells found are chiefly of the polynuclear amphophile type. Mononuclear cells phagocytic for leukocytes occur. The meningitis is rarely so voluminous as the ependymitis. Numerous polynuclear leukocytes follow the cortical vessels; and it is not unusual to find leukocytes of the amphophile type in close apposition to nerve cells, as well as free in the tissue of the upper cortical layers.

The brain of the guinea-pig nine days after inoculation shows little exudative process except about certain vessels, where rare polynuclear leukocytes occur with fairly numerous cells of the mononuclear series. Occasional cells phagocytic for chromatic material occur, besides a few pigment-bearing cells. The exudate is, as a whole, slight.

Few traces of inflammation are demonstrable in the brain of a guinea-pig one month after inoculation. The brain substance shows no alteration beyond a few areas of chromophilic nerve cells mentioned below. Neuroglia fibrillæ are demonstrable beneath the pia, but in quantity which is within the normal limits for the guinea-pig by the methods used. The ependyma shows no change. The pia mater contains a few pigment-bearing phagocytes, a few lymphoid and plasma cells, and relatively many eosinophilic polynuclear leukocytes.

The examinations were throughout controlled by cultures from various organs, the brain, and the site of operation in the subdural inoculations. A surprising proportion of negative cultures was obtained from the brain even where lesions of the appropriate age could be determined. The tenuity of the lesion makes scaring risky. Perhaps cultures from the ventricle are preferable in cases where the process has reached the ventricle. The above descriptions have been founded on cases in which the bacterial diagnosis was secure. The organs of the trunk were examined in many cases to make sure of the pyæmia.

Mention may be made of a frequent lesion in the guinea-pig brain which remains obscure. To be distinguished sharply from the focal occurrence of condensed, deeply staining nerve cells, and from the occurrence in compressed material and at the edges of some sections of groups of similar cells which are more or less clearly a product of technical error, are certain foci of contracted, angular or sub-angular, deeply staining nerve cells of the cortex. In one case there were deposited in the cell bodies of one of these chromophilic

foci dots staining by the phosphotungstic-hæmatein method. These foci of chromophilic cells occur, as far as we have yet found, without definite relation to the bacterial inoculations, but are not characteristic of the brain of normal pigs. The process is a little more frequent in groups of Purkinje cells.

RESUME. 1. The staphylococcus pyogenes aureus produces in the meninges and brain substance of man a type of inflammation in which hæmorrhage is prominent.

The picture post-mortem in man varies from red softening or multiple ecchymosis and small abscess to frank and sometimes voluminous hæmorrhage. The site of election for the hæmorrhagic lesions is the subcortical region, supplied by the long or medullary branches of the cortical vascular system.

The histological picture varies from diapedesis and slight leukocyte emigration to abscess and acutely destructive hæmorrhage with phagocytosis. Collections of mononuclear cells phagocytic for cells and cell detritus often quite obscure the acute inflammatory appearance of the lesion.

Six fatal cases in man were examined, all but one cases of general infection with the staphylococcus aureus.

A history of antecedent disease was the rule. The syndromes, which were chiefly of sudden onset and rapid course (three to fifteen days), were pyæmic, meningitic, or cerebral in type. The cases of slower course were the most plainly cerebral.

2. The staphylococcus pyogenes aureus produces in the brains of guinea-pigs an inflammatory process which tends to subside within a limited period (two weeks), and, as a rule, remains without clinical signs throughout.

No hæmorrhages other than miliary perivascular ones were observed in the guinea-pig. The lesions are seldom grossly evident.

The cell pictures are of meningitis (discernible in six hours), ependymitis (twelve to fourteen hours), and exudation into the brain substance (twenty-four to forty-eight hours).

The four and five day cases show numerous cells of the lymphocyte series as well as mononuclear cells phagocytic for exudative cells. Examples of such phagocytic cells have been found as early as twenty-four hours after inoculation.

The exudation into the meninges is discernible earlier, and its traces are demonstrable later, than are the processes in the ependyma and the encephalon; but the meningitis is never so extensive or striking a process as the encephalitis or the choroiditis.

In two weeks to a month there is little sign of the previous infection.

3. The staphylococcus pyogenes aureus, of the strains and in the doses experimentally used, produces in the guinea-pig a curable encephalitis, that is a process which in logic is termed reversible. The same organism produced in our human cases extensive

brain lesions which surely look as a group irreparable. Perhaps, however, there are in man also certain cases of encephalitis which reverse themselves, and which in their course are taxed with being "functional" diseases and furnish "functional" symptoms during and after tissue repair.

We wish to thank Drs. Mason, Shattuck, Sears, and Coolidge for the use of their clinical records, and Drs. Brinckerhoff, Thompson, and Wolbach for the anatomical data in their autopsies. Drs. Councilman and Mallory have looked over the histopathological work, and Dr. W. N. Bullard has interested himself in its neurological aspect. The work was done under the Bullard Gift to the pathological department of the Harvard Medical School for 1904.

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## PRIMARY SPLENOMEGALY—GAUCHER TYPE.\*

REPORT ON ONE OF FOUR CASES OCCURRING IN A SINGLE GENERATION  
OF ONE FAMILY.

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CLINICAL (DR. N. E. BRILL). Under the caption of primary splenomegaly have been heaped together indiscriminately a large variety of non-leukæmic enlargements of the spleen developing with or without anæmia. Osler, in an attempt to establish order out of chaos, suggested calling the cases of enlarged spleen associated with an anæmia of the chlorotic type and with hemorrhages, but unaccompanied by a leukocytosis, splenic anæmia, adopting as the cognomen the term first used by Griesinger for the splenic variety of Hodgkin's disease. He insists that these cases in their evolution present a terminal stage characterized by secondary cirrhosis of the liver associated with jaundice and ascites, which Banti described as constituting a disease *sui generis*, and which cases have been known as those of Banti's disease. But even with Osler's limitation, under the term of splenic anæmia, there have been associated diverse splenic enlargements, differing both in their clinical and pathological conditions, such as the cases described by Sippy,<sup>1</sup> Osler,<sup>2</sup> Rol-

\* An abstract of this report was presented at a meeting of the New York Pathological Society on December 14, 1904.

leston,<sup>3</sup> Taylor,<sup>4</sup> Gilbert and Fournier,<sup>5</sup> Stengel,<sup>6</sup> and others. Much more work will have to be done, many more clinical and pathological investigations will have to be made, before a satisfactory classification of the varieties of types of so-called splenic anæmia can be agreed upon.

The writer insists that the type of splenomegaly first described in 1882 by Gaucher<sup>7</sup> as "Splenomégalie Primitive—Primary Epithelioma of the Spleen," and after him by Picou and Raymond,<sup>8</sup> Collier,<sup>9</sup> and Bovaird,<sup>10</sup> ought not to be included in the category of splenic anæmia, because its pathology is unique and typical and the clinical picture so distinctive that it can be recognized during life. It was from the clinical picture presented by the patients whose histories I reported in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for April, 1901, that I was able to predict that my cases\* belonged only to the class described by Gaucher as splenomegalie primitive. Indeed, one of the distinctive features of this class, which alone might separate it from all the cases belonging to the category of splenic anæmia is the enormous increase in the size of the liver, which almost equals the colossal size of the spleen.

For the benefit of those who have not access to the original article, a *résumé* of the clinical data of the case which forms the topic of this report is herewith given; for full details the reader is referred to the original publication. It is the first male case ever reported in literature:

Maximilian R., born in 1870, had suffered from the common infectious diseases of childhood, but never had malaria, rheumatism, or tuberculosis. He had not been rachitic and never contracted gonorrhœa or syphilis. After his ninth year he was a sturdy, muscular, healthy chap, and never was ill outside of an occasional attack of bronchitis. The only features of an abnormal nature which the patient himself observed was a tendency to sweat easily, the frequent presence of sudamina, even in winter, and a persistent patch of erythematous papules which extended from the malar prominence of one side across the skin covering the nasal bone to the same prominence on the other side, most intense, however, on the bridge of the nose. The latter developed about his fourteenth year, and, notwithstanding treatment by skin specialists, was persistent. In 1885, when he came under my observation, this patch was prominent. No signs of splenic enlargement appeared until 1889. Patient felt in perfect health all the years since his ninth. There were no pains in the splenic region at any time up to the date of the detection of an enlarged spleen. Since 1889, after an apparent initial slight reduction in the size of the spleen, there had been a steady, slow, progressive increase in size of that organ, with occasional attacks of epistaxis. In 1899 the first absolute signs of liver enlargement

\* The disease has since been discovered by me in another sister, who constitutes the fourth member of the one generation of the family thus afflicted.

became demonstrable, and about this time was noticed a peculiar hard, pale, ochre-colored, wedge-shaped infiltration of the sclerotic of the nasal side of each eye, the base being limited by the cornea, the apex extending toward the nasal angle, thus differing from the ordinary pinguecula.

While feeling in perfect health the patient was losing weight very slowly but progressively. Between 1899 and 1900 the skin of the face, neck, and hands began to assume a dusky, light yellowish-brown tint. Wherever the skin was not exposed to the light and air it was perfectly normal in color. There was an entire absence of jaundice; examination of the blood and urine showed no bile.

Frequent blood examinations were made, blood counts dating from 1893, and showing a normal red and white count, and normal proportions of polynuclear neutrophiles, small and large mononuclears and eosinophiles. The hæmoglobin up to 1900 was never lower than 80 per cent. by Gowers' instrument.

The progress of the disease became rapid from August, 1900, when the patient was seized by an attack of acute colitis, starting with a chill, and followed by hyperpyrexia and diarrhoea, the movements finally becoming bloody and composed then of mucus and sanguineous fluid. Immediately after convalescence hemorrhagic furuncles appeared on the legs, thighs, trunk, arms, and forehead, leaving behind them, when healed, permanent pigmented spots at the site of each furuncle. Excepting these spots and the peculiar change in color of the face and hands, there was no pigmentation anywhere of the skin or of the mucous membranes accessible to inspection. Later in the year the first signs of petechiæ appeared, three on the thorax.

From January, 1902, to May, 1902, there was very little if any change in the condition of the patient. In May he began to complain of pain in the lower end of the left tibia. Physical examination at the seat of pain revealed nothing, there being no swelling, redness, or tenderness.

On June 6, 1902, he was seized by an attack of malarial infection, with the usual signs of the tertian type; plasmodia were found in the blood. A course of quinine dissipated the organisms. Epistaxis, which had not been frequent in the past, now became more so, and the blood examinations revealed a steady decrease in hæmoglobin to 45 per cent., and a slight increase in leukocytes, 8240; the red cells being diminished, 3,420,000. The red cells showed a few normoblasts (August 1, 1902). He complained less of pain in the lower part of the tibia; occasionally this pain disappeared entirely, even for a month at a time. During the attack of malarial infection there was no demonstrable increase in the size of the spleen.

In September the patient was so well that he again attended actively to business. He remained in a condition of relative well-being throughout the rest of the year and the first half of the follow-

ing year, 1903. During these nine months he had but four attacks of epistaxis. In April, 1903, he began to complain again of the pain in the neighborhood of the ankle and also about the left knee. There were no local signs of swelling, etc., and no indications of a hæmarthrosis. A blood examination at this date revealed the following: red cells, 4,400,000; white, 5240; hæmoglobin, 55 per cent.; polynuclear neutrophiles, 65 per cent.; small mononuclear, 26.5 per cent.; large mononuclear, 6.5 per cent.; transitional forms, 1 per cent.; eosinophiles, 0.5 per cent.

In June, 1903, in the warm spell, his sudamina became pronounced, a few miliaria becoming hemorrhagic; the erythematous patch on the nose became more livid. The pain in the left knee and ankle, however, disappeared. The heated term weakened him considerably, and he left town, spending the next three months in the mountains, where he felt very well.

On his return examination revealed a slight increase in the size of the spleen, its anterior border extending 3 cm. beyond the middle line; the upper border (dulness) was at the fifth rib in the mid-axillary line; the posterior border could be felt in a line with the angle of the scapula about 4 cm. from the lumbar spines, and became lost to the touch behind the iliac crest. The liver had relatively increased more in size. Liver flatness was elicited at the fourth rib, lower border palpable 4 cm. below the level of the umbilicus, extending below the iliac crest in the midaxillary and post-axillary lines. His chest and abdomen were more bulging than ever.

*September 27, 1903.* Red cells, 4,200,000; white cells, 6200; polynuclears, 70 per cent.; small lymphocytes, 22 per cent.; large lymphocytes and transitionals, 7 per cent.; eosinophiles, 0.5 per cent.

*Heart.* Loud systolic murmur at apex and over pulmonary area; upper border of cardiac dulness at lower border of second rib; right border at right sternal line; apex in third interspace.

*November 17th.* A moderately severe epistaxis.

*27th.* A few petechiæ are noted on the dorsum of each hand; none on conjunctivæ. Hæmoglobin, 50 per cent. Patient has a ravenous appetite. Again complains of pain in left knee and ankle. He, however, has been taking long walks daily. No demonstrable increase in size of spleen or liver.

*January 6, 1904.* First appearance of ecchymosis—one ecchymotic spot on left lower leg near the end of the fibula and one on dorsum of left foot, each about 2 cm. in diameter. Emaciation much more marked since last note. Hæmic murmur increased in intensity. Hæmoglobin, 45 per cent. No epistaxis since November 17, 1903, yet a gradual hæmoglobin reduction. No ascites. Has had dyspeptic symptoms, perhaps partly due to the excessive amount of food he has been taking.

*March 12th.* Patient began to complain of dyspnœa and fever, with great weakness. Temperature, 101°. Limit of cardiac dulness

considerably to right of sternum; left border not definable, owing to interference of spleen; apex beat feeble and in third interspace. Same hæmic murmur. No recognizable increase in spleen and liver.

13th. Patient feeling better. Temperature, 100°; two ecchymotic (fresh) spots over right tibia; another on dorsum of left foot. Dyspnoea; respirations, 34. Says he feels comfortable.

20th. Since last note normal temperature until yesterday. To-day increased difficulty in breathing, pain behind sternum, sticking and rubbing in character; chills; respiration 38 and labored; pulse 116; temperature 103°. Apex beat cannot be felt; to-and-fro superficial friction at junction of third right rib with sternum. Diagnosis of pericarditis, with probable bloody effusion. From this day on fever persisted, weakness became extreme, the patient became irritable, objected to further blood examinations. Signs of fluid in peritoneal cavity. Dyspnoea more extreme, the pericardial friction more rough and superficial, the pulse became weaker; exitus, with mental faculties preserved to final moment, on March 30, 1904.

*Negative Symptoms.* Urine never contained bile; negative examination for pathological urobilin (Jaffé); never any casts; never albumin; urea never much above normal limits; highest 3.4 per cent. Ascites never present, except two days before death. Œdema absent. Jaundice absent throughout. Superficial lymph nodes never enlarged.

*Blood.* Never contained bile; coagulation time gradually increased in length toward terminal stage of disease to fourteen minutes, first examination in 1899 being three minutes.

*Hemorrhages.* Epistaxis was the only form. The attack of colitis associated with bloody stools cannot be considered as a melæna. Toward the last two years of life petechiæ and ecchymosis, few, however, in number.

*Discoloration of Skin.* Limited to face and neck, wrist and hands. Skin of body not discolored. Discoloration not that of Addison's disease; color, yellowish-brown. It would appear as if the light and air had some influence in changing the tint of the exposed parts. The color is not one due to ordinary exposure; it remained permanent. Bovaird mentions bronzing of the face and hands of his patient. Bronzing is not applicable to this case.

Local pain over spleen and liver absent, though such could be elicited by pressure.

No bone tenderness; pressure over lower end of femur and tibia relieved the pain when present in those regions.

No feeling of being sick except during an intercurrent affection—colitis, malarial disease, terminal pericarditis—on the contrary, a feeling of well-being.

Owing to the unusual importance of this case, I have been happy to call into its collaboration the aid of Dr. Mandlebaum, who made



the histological examination and who prepared the photomicrographs, and of Dr. Libman, who made the autopsy.

REPORT ON POST-MORTEM EXAMINATION MADE MARCH 31, 1904, 11.45 P.M.—No rigor mortis; body emaciated; pupils large; yellowish-brown discoloration of face and hands. A few small lymph nodes in both axillæ the size of peas; in supraclavicular regions a few half the size; the same in the epitrochlear and inguinal regions. Panniculus adiposus atrophic; muscles of the abdominal wall succulent. In the abdomen 1000 c.c. of hemorrhagic fluid, chocolate in color. The body musculature is atrophic, pale.

Old and recent adhesions over liver; omentum adherent to anterior surface of the spleen; the spleen at its upper pole is adherent to the surrounding tissues.

Diaphragm on the right side at the third rib and on the left at the fourth rib. Lower part of the chest markedly expanded. All the intra-abdominal veins are distended.

Anterior mediastinal nodes enlarged the size of peas, yellowish-brown in color; on section there are pinpoint hemorrhagic areas.

*Lungs.* No fluid in pleural sacs; both lungs congested, lower lobes compressed. Lingula emphysematous. Bronchial nodes moderately enlarged and anthracotic.

*Pericardium.* Very markedly distended by 2 litres of very bloody fluid. Microscopic examination of the fluid reveals altered erythrocytes only. The visceral pericardium is coated by a layer of shaggy fibrin, which is easily removed.

*Heart.* Small; old thickening of posterior visceral pericardium; right auricle dilated. Tricuspid orifice admits three fingers; the valve is slightly thickened. The wall of the right ventricle is thin. The pulmonary valves are negative. The left ventricle is small; the auricle dilated. The heart muscle is firm, brownish. The coronaries and aorta show no lesions. There are no congenital defects.

*Esophagus and Stomach.* Marked congestion. Stomach is dilated.

*Spleen.* Immensely enlarged, filling the larger part of the abdominal cavity. The weight is 5280 g. (11 pounds). It measures 40 x 20 x 14 cm. The organ is of an elongated ovoid form. The surface as a whole is of a reddish-brown color and shows marked recent and old perisplenitis. There are irregular depressed areas on the surface, evidently the result of infarctions. The organ is very firm. On section the color is that of chocolate, but here and there are lighter areas of a grayish-red color. The pulp is moderately swollen. There is a large number of old and recent infarctions, mostly peripheral. In some sections the whole periphery is made up of infarcted tissue; some of these infarcts are surrounded by hemorrhagic zones; most are anæmic and look cheesy. In the lower pole there is a white area about 1.5 cm. wide, crossing the entire width of the spleen. Where the pulp is less swollen the con-

nective tissue is seen to be decidedly increased. In the pulp are a number of small hemorrhages. The splenic vessels show no changes. At the lower part there is a globular mass of splenic tissue attached by a flat pedicle to the main organ; it measures 4 x 6 cm. On section it is dark brown in color, with grayish markings.

*Liver.* Weight 4.8 k. (10 pounds). It measures 35 cm. in width; both lobes are 27 cm. in length; thickness of the organ is 13 cm. There is marked old and recent perihepatitis. The surface is pale reddish-brown, with irregular white and dark-brown markings. The right lobe is oblong; the left ovoid; the free border is rounded. On section the organ is quite firm. As a whole it is chocolate-colored; the cut surface is rather granular. Throughout the liver are irregular white markings, varying in diameter from 0.5 cm. to 2 or 3 cm., which, for the most part, are ramifying. They do not seem to bear any definite relation to the lobular markings. In both lobes, but especially in the right, there is a number of fine hemorrhages. The portal vein and the gall-ducts show no changes. The gall-bladder is distended by a large amount of very dark bile. The wall appears to be normal.

*Kidneys.* Left: weight, 150 g., capsule markedly adherent; moderate lobulation; surface slightly granular; veins injected. On section the organ is quite firm. The cortex is narrow, but swollen; the markings are poor. There is a hemorrhagic area in the labyrinth. There are uric acid deposits in the cortex and in the papillæ; also lime infarctions in the latter. In the pelvis there are petechiæ and one large hemorrhage. Right: weight, 120 g.; surface the same as that of the left kidney; cortex, yellow in color. The organ is succulent; there are hemorrhages in the pelvis. Just external to the pelvis there is a border of very succulent, reddish tissue, varying in width from 0.5 cm. to 1 cm. There are uric acid and lime deposits as in the left kidney.

*Ureters.* Negative.

*Adrenals.* Negative.

*Pancreas.* Negative.

*Small Intestine.* The walls of the jejunum and duodenum show blood injection; the contents are tarry. The mucosa of the ileum is swollen, and there are hemorrhages in the wall.

*Colon.* Small effusion of blood in and under the mucosa of the ileocaecal valve and the caecum. The contents of the large intestine are hemorrhagic. No evidences of lymphatic hyperplasia. The wall of the rectum is injected.

*Bladder.* Marked injection of the vessels of the trigone. Prostate normal in size; color, yellowish.

*Lymph Nodes.* The mesenteric nodes moderately enlarged; they look like the prevertebral nodes. The latter vary in size, the largest being about the size of a large bean. They are fairly soft, ochre in color, and show some hemorrhagic markings.

*Bone-marrow of Femur.* Uniformly dark red in color; quite firm; no changes in bone.

*Thoracic duct* is formed by two separate channels, which coalesce just below the diaphragm.

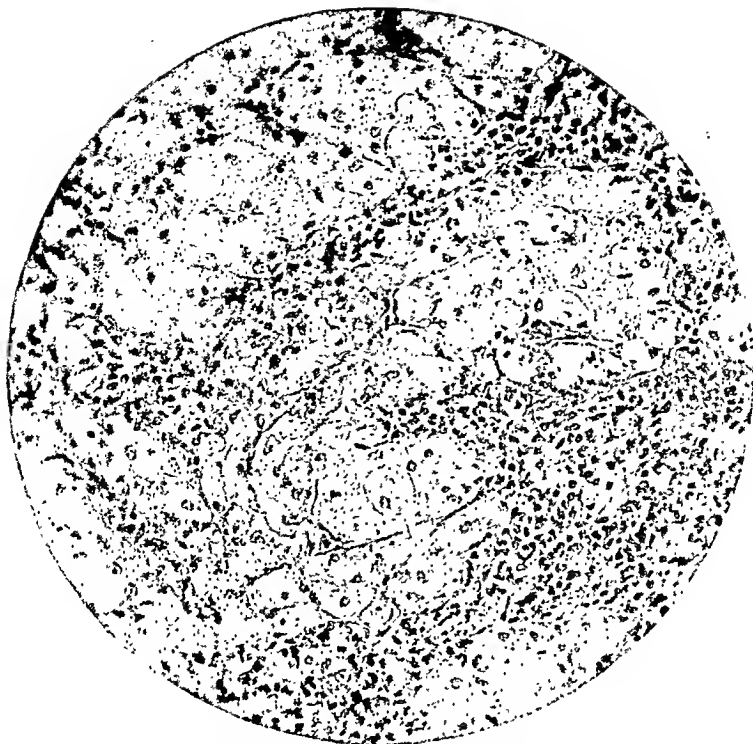
*Bacteriological Examination.* Cultures made from the heart blood remain sterile. Those made from the spleen show the staphylococcus albus.

**MICROSCOPIC FINDINGS.** Pieces of tissue from various parts of the organs were fixed in Zenker's solution, saturated sublimate, formalin, alcohol, Müller's fluid, and Orth's solution, and were embedded both in celloidin and paraffin. The ordinary histological stains were employed, also iron hæmatoxylin, Biondi-Heidenhain, Pappenheim's methyl-green pyronin, Mallory's connective-tissue stain, Unna's polychrome methylene blue, Weigert's modified Van Gieson's stain, and others.

*Spleen.* Certain peculiarities are found in sections from different parts of the organ. Many dense bands of fibrous connective tissue are seen surrounding certain parts of the splenic tissue. In places where these bands are less dense, the individual connective-tissue fibres are seen to be slightly separated from one another by a faintly staining homogeneous substance containing a few mononuclear cells and giving the usual appearances of oedema. Occasionally an area is found near the margin of a band of connective tissue, where the fibres are more widely separated, giving rise to small, irregularly shaped spaces or meshes. As a rule, these spaces contain a few normal pulp cells, though here and there an endothelial cell of the type described below is seen, entirely surrounded by delicate connective-tissue fibres. The capsule and the trabecular arrangement are quite normal, with the exception of certain pigment, which will be mentioned below, and a slight increase in the amount of connective tissue. The infarcts are of the usual anæmic variety. Some of these contain areas of necrosis, with many slit-like openings, due, in all probability, to the presence of cholesterin crystals. In some of the necrotic areas the remnants of alveolar spaces filled with endothelial cells, as described below, can be seen.

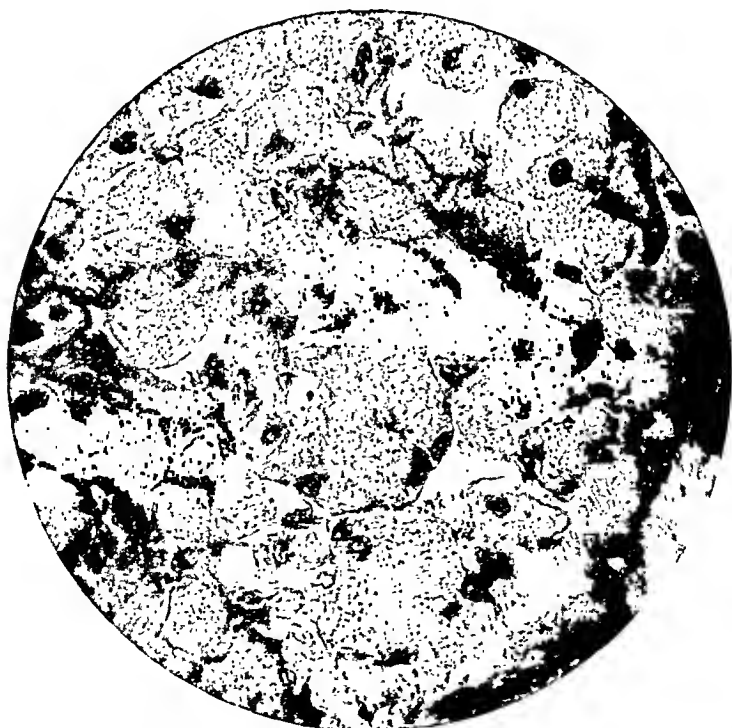
Scattered throughout all the sections are large masses of cells which require further description and which seem to be the principal and characteristic feature of the disease. The cells are found mainly in large, irregularly shaped, alveolar spaces, whose walls are composed of delicate connective tissue lined by endothelium. Fine capillaries are seen in the walls in places where the latter are somewhat thickened. These alveolar spaces measure from  $130\mu$  by  $269\mu$  to  $95\mu$  by  $108\mu$ , respectively. Many variations in size occur between these extremes. The alveolar spaces or pulp spaces may be looked upon, according to Weidenreich,<sup>11</sup> as the venous capillaries of the spleen. In some places a direct connection between adjacent alveoli is found to exist.

FIG. 1.



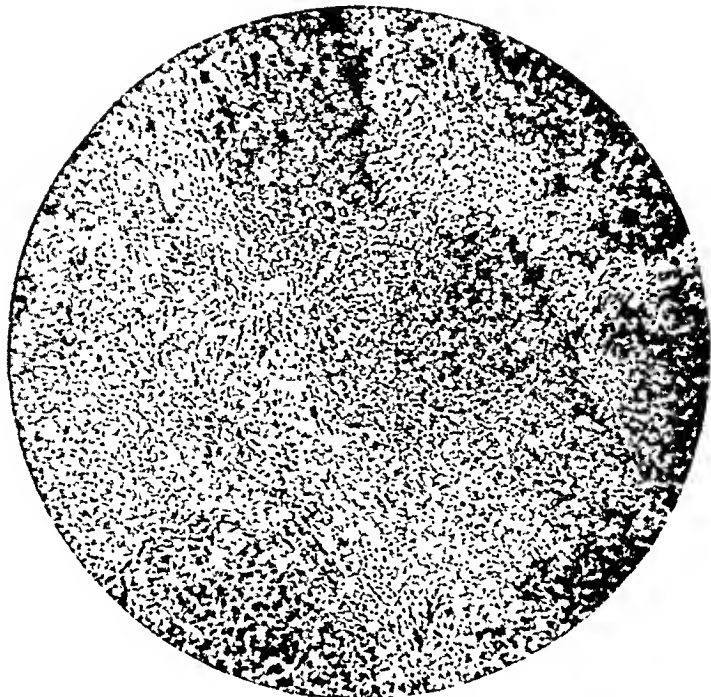
Photomicrograph of spleen, showing the alveoli filled with endothelial cells.  $\times 250$ .

FIG. 2.



Photomicrograph, showing the general granular and streaked appearance of the endothelial cells.  $\times 500$

FIG. 3.



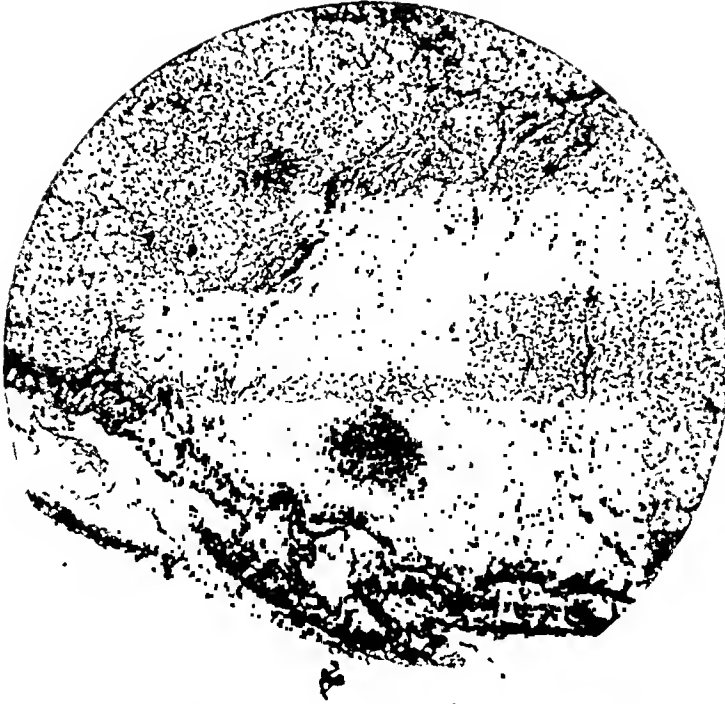
Photomicrograph of liver, low power, showing the increase in connective tissue and the general appearance of diffuse cirrhosis.

FIG. 4



Photomicrograph of liver node, showing the pigment distribution and the endothelial hyperplasia

FIG. 5.



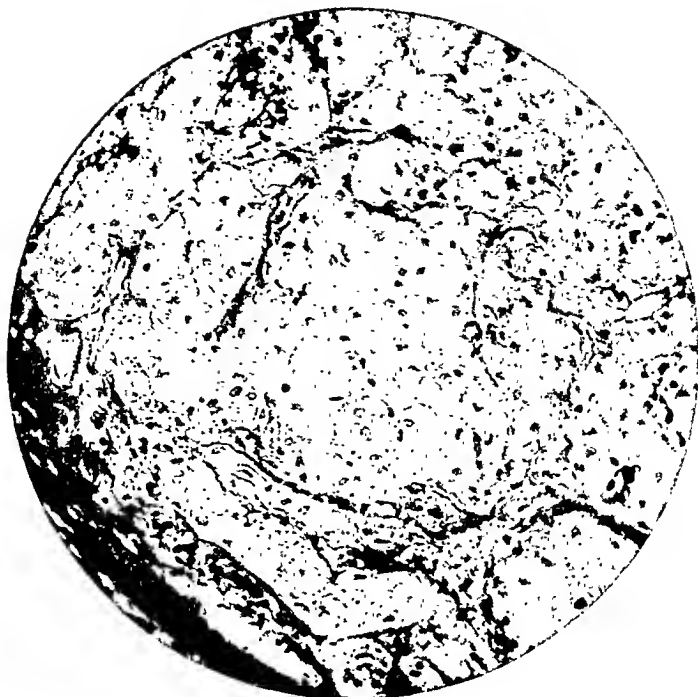
Photomicrograph of lymph node, low power, showing remnants of two follicles and absence of normal lymphoid tissue.

FIG. 6.



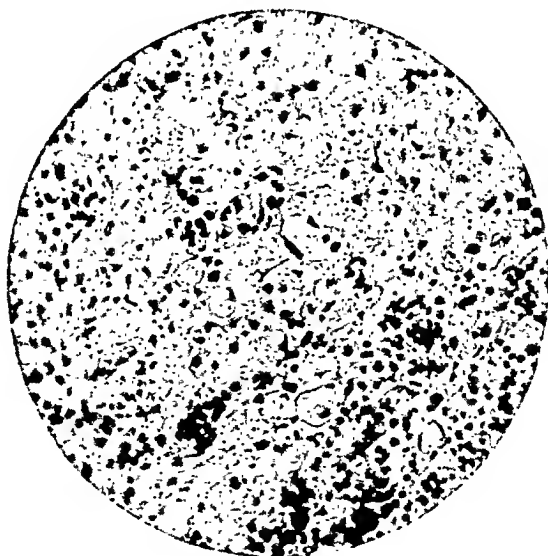
Photomicrograph of lymph sinus containing pigment granules and endothelial cells in its lumen. On the right is the connective tissue of the capsule; on the left are endothelial cells arising from the wall. 500.

FIG. 7.



Photomicrograph of lymph node, showing the endothelial cells arising from the reticulum, and the general type of the multinuclear endothelial cells.  $\times 250$ .

FIG. 8.



Photomicrograph of bone-marrow, showing a small group of endothelial cells.  $\times 250$ .

The endothelial cells which line these spaces can readily be seen. In some places they are of normal appearance; in other places they are distinctly swollen. Occasionally a few very delicate connective-tissue fibres may be found within the alveoli. The endothelial cells filling these spaces are so abundant in number that in many places it is impossible to distinguish any of the normal splenic tissue. Only here and there can a single Malpighian body be seen. These bodies have no degenerative changes, but the central artery shows a slight thickening of its walls. Here and there a few connective-tissue fibres can be found in the Malpighian bodies themselves, principally at the periphery. The cells are found both lying free and attached to the wall of the spaces, and their size and shape corresponds to the amount of pressure exerted upon them. For the most part, the cells resemble swollen endothelial cells. They are, as a rule, quite large in size, round, oval, or polygonal in shape, depending upon the number in a given space (Fig. 1). The cell bodies stain faintly, but distinctly with eosin or picric acid, and show a slightly granular appearance of the cytoplasm, but no degenerative changes. The outline of the cell body is usually well preserved. In thin paraffin sections a distinct network of fine linear markings can be seen in some of the cells; with the high power these fine lines seem to be composed of minute dots. In other cells very delicate wavy lines are distinguished, arranged in a more or less concentric form, giving a streaked or wrinkled appearance to the cell. This appearance of the cytoplasm is well brought out by Mallory's phosphomolybdic acid hæmatoxylin stain. Fig. 2 shows the general granular and streaked appearance of the cells under high amplification. Vacuoles are not uncommon, as many as four or five being present in some of the larger cells. In favorable parts of the sections the cells can be seen arising directly from the endothelial lining of the pulp spaces, or, more properly, venous capillaries. In size the cells vary from  $17.4\mu$  by  $21.75\mu$ , to  $34.8\mu$  by  $47.85\mu$ , respectively. Nuclei of a relatively small size are seen in the cells. The average measurement is  $5.43\mu$  by  $8.7\mu$ . These are found either centrally placed or near the periphery. Some of the cells contain three or four nuclei, but the number of nuclei found in a single cell does not correspond always to the size of the latter, for some of the very largest cells contain but a single nucleus. The nuclei vary considerably in size, from small, round, deeply staining bodies rich in chromatin, to larger, irregular forms staining rather freely. Some of the nuclei show atypical mitotic changes, and a few contain distinct nucleoli. No typical giant cells are seen in any of the sections. Here and there the pulp spaces are seen well distended with red blood cells and normal adenoid tissues. Some of these spaces contain but a few endothelial cells; others show a relatively large number. Many of the bloodvessels throughout the sections are surrounded by a slight increase of connective tissue. A few veins, however,



are noted, whose walls appear quite normal. These are filled with blood.

Light, brownish-colored pigment particles are scattered here and there in the pulp spaces and also in some of the pulp cells. Throughout the trabeculae fine granules of brownish-yellow pigment are seen, in long spindle-form arrangement, corresponding to the capillaries and also lying free between the connective-tissue fibres. Sections treated with potassium ferrocyanide and hydrochloric acid give the characteristic iron reaction. Sections were stained for bacteria, but none could be discovered. Neither could any bodies be found resembling protozoa.

*Liver.* The capsule is much thickened and contains many pigment granules. A striking feature in all the sections is the enormous increase in the amount of interlobular connective tissue throughout the organ, without any apparent influence upon the liver cells themselves. This interlobular structure is composed of very delicate connective-tissue fibres containing numerous capillaries and some pigment. With Mallory's aniline-blue stain a few very fine fibrillae can be seen extending into the lobules here and there. The bile-ducts are not increased in number and appear quite normal. Under the low power the general picture is that of a diffuse hepatic cirrhosis (Fig. 3). The liver cells, for the most part, are normal, though occasionally a cell is seen containing minute fat-droplets, and a few nuclei show the usual appearance of regeneration.

The peculiar endothelial cells described in the spleen are also found in abundance in this organ. A few are seen in the lobule proper, but the majority are situated in interlobular connective-tissue spaces. In the lobules these cells are, for the most part, situated in the capillaries at the periphery, though now and then single cells can be found in the deeper parts of the lobule surrounded by liver cells. The individual endothelial cells can be made out quite readily, though they are not so clearly defined as in the spleen. In the interlobular connective-tissue spaces the cells are so intimately fused together that their recognition is somewhat more difficult, but sections treated by Weigert's modified Van Gieson's stain show the cell bodies quite distinctly. In every other respect the cells are identical in appearance with those found in the spleen. In a few places there seems to be a tendency for these cells to invade the lobule itself, but, for the most part, the cells seem to be confined to these spaces and in intimate union with the connective-tissue fibres. The pigment in this organ responds also to the test for hæmosiderin. The bloodvessels appear quite normal, as a rule. Some of the arteries have slightly thickened walls.

*Mesenteric Lymph Nodes.* The capsule and trabeculae are sharply defined by the large amount of pigment which outlines their course. Throughout the nodes the trabeculae are deeply pigmented, but not otherwise affected (Fig. 4). The pigment is dark brown in

color, and in the thinnest sections can be seen either as elongated whetstone-shaped crystals or as fine amorphous particles. Smaller masses of pigment are also seen distributed in the cortical and medullary portions of the node. The lymph sinuses are all filled with pigment. Iron reaction is present. The nodes are so changed in general appearance and structure that the usual characteristics have entirely disappeared. A section through the central portion of a somewhat enlarged node shows less than ten follicles. The germinal centres are not well marked, but otherwise the follicles are quite normal, excepting that occasionally a few delicate connective-tissue fibres may be seen in the follicle near its periphery. Only here and there are small remnants of normal lymphoid tissue seen (Fig. 5). The medullary portion of the node is somewhat less affected than the cortical substance. The reticulum of the organ is well preserved.

The entire node is practically transformed by the presence of endothelial cells, such as were described in the spleen and liver. With the exception of the connective-tissue structures, follicles, and small remnants of lymphoid tissue, the whole section is but one mass of these cells. Notwithstanding this fact, the individual cells are most distinctly outlined and clearly seen and show but a slight tendency to fuse together. The cells can be seen arising from the walls of the lymph sinuses (Fig. 6), and from the reticulum throughout the node (Fig. 7). In size, shape, structure, and staining properties, the cells are identical with those described above. A few very large cells measuring  $39.15\mu$  by  $56.55\mu$ , are present. Some contain as many as nine nuclei. These are not arranged in any particular form, and no cells are found presenting any of the usual appearances of giant cells. The bloodvessels are surrounded by a slightly increased amount of connective tissue, but show no other changes.

*Bronchial Lymph Nodes.* These nodes are affected in a like manner. The endothelial cells are of the same general structure and appearance as in the mesenteric lymph nodes and distributed in a similar manner, but they are not present in such great numbers. Here and there small areas of quite normal adenoid tissue are seen, with fairly well-preserved follicles. Pigment is also present and is identical in color, distribution, and reaction with that found in the mesenteric nodes. Besides this, a moderate amount of anthracosis is present. The capsule and trabeculae show a rather marked increase in amount of connective tissue. The bloodvessels are prominent throughout and well distended with blood. Their walls are somewhat thickened, but show no degenerative changes.

*Retroperitoneal Lymph Nodes.* The same process is also found here. The general picture is identical, but a few slight differences may be noted. The capsule is more markedly thickened than in the other nodes, but the pigment, particularly in the lymph sinuses, is not as prominent. Surrounding the follicles are quite a number

of small capillaries, and the margins of the follicles show the presence of young connective-tissue fibres. Numerous small bloodvessels, mostly arteries, are seen. These vessels show hyaline changes. In parts of the section degenerative processes have occurred, so that many of the endothelial cells, as well as the adenoid tissue, do not stain distinctly. The entire process in these nodes seems somewhat older than in those described above.

*Bone-marrow.* Cells identical with those in the above-described organs are found in abundance in the bone-marrow. There is considerable variation in the size of the cells in the bone-marrow as compared with those found in the other organs, but the general characteristics are preserved. Vacuoles are common in these cells. No forms are found with an excessive number of nuclei, neither are any of the very large types, such as were described in the lymph nodes, to be seen. Occasionally a large mass of these cells is noted, but for the greater part they are found either singly or in groups of from four to ten cells (Fig. 8). In the latter instance the cells are always found in intimate relationship with the walls of the capillaries or attached to the connective-tissue reticulum. The larger masses cannot always be seen to have such a relationship, and occasionally they are found surrounded by a considerable number of red blood cells. In a few places the cells are distinctly seen within the lumen of dilated capillaries.

A large number of stains were employed in the examination of these sections, but the Biondi-Heidenhain method gave the best results, bringing out the connective-tissue reticulum with much clearness. A few polynuclear leukocytes, some of which show eosinophile granulations, are present, also normoblasts and giant cells in considerable numbers. The larger bloodvessels appear normal. No pigment is present.

Spreads made from the bone-marrow by Dr. Libman, and stained with eosin-haematoxylin, Ehrlich's triacid stain, Jenner's stain, and Wright's stain, show the following: There are present many erythrocytes; these are of about the normal size or larger (macrocytes). Slight poikilocytosis is also noted. Normoblasts are very abundant, showing karyokinetic and karyolytic changes. Small and large lymphocytes and mononuclears are present; also polynuclear neutrophilic and eosinophilic leukocytes, but the main bulk of leukocytes is made up by neutrophilic and eosinophilic myelocytes. Some of these are quite large, as are also some of the polynuclear leukocytes. With the Wright stain azurophile granules are seen in a few lymphocytes. Mastzellen are not to be found. The large endothelial cells have basophilic nuclei; their cytoplasm stains slightly basophilic and faintly acidophilic. Giant cells are abundant.

The spreads of the spleen and liver show no nucleated erythrocytes, no giant cells of the type seen in the marrow, and no myelocytes. The cytoplasm of a few of the endothelial cells is granular-

looking, the granules taking on an appearance resembling neutrophilic granulations, but they do not impress one as possessing true granulations.

*Lung.* The vessels are all distended with blood. The vesicles are compressed in a great measure and show evidences of œdema. A moderate amount of fibroid induration is present. The sections show a moderate degree of anthracosis, and some hæmatogenous pigment is seen scattered through the organ.

*Heart.* The pericardium shows a recent serofibrinous exudate with the production of young connective-tissue fibres. In the meshes of this exudate are a large number of small round cells and some red blood cells. Many newly-formed capillaries are also noted. The muscle fibres of the heart show considerable parenchymatous degeneration; also a moderate amount of brown atrophy. No changes are seen in the bloodvessels.

*Kidney.* Sections show the usual picture of a chronic interstitial nephritis. Bowman's capsule is much thickened, and here and there the glomeruli are entirely replaced by fibrous tissue. The tubular epithelium is coarsely granular, and the nuclei are occasionally missing. The epithelium shows vacuoles in places. There is also some increase in connective tissue between the tubules, and a few areas of infiltration by small round cells are seen. The vessels are the seat of endarteritis, and the sections also show a slight amount of congestion. Small deposits of lime salts are present. The right kidney shows rather more congestion than the left, and in the medulla is a large hemorrhagic area containing blood pigment and surrounded by a zone of chronic inflammatory tissue.

*Pancreas.* This organ shows no lesion.

*Adrenal.* The sections are normal.

*Colon.* The mucosa is somewhat congested. In the submucosa are many dilated veins filled with blood. Otherwise the sections are quite normal.

While the study of this case was nearing completion, the sister of this patient met with a fatal accident. Her organs are now being studied. Owing to the fact that these may give additional information, we shall reserve our full discussion of the features of these cases to a subsequent publication.

We may state, however, that our findings enable us to place this case in the group described by Gaucher, Picou and Raymond, Collier, and Bovaird. The spleen and liver show the same changes as described by Gaucher, but he has not reported fully in regard to the lymph nodes. Picou and Raymond report simply on the spleen and lymph nodes, as in their case the spleen was removed at operation. Our findings correspond with theirs in nearly every respect. The spleen in Collier's case is also identical. Bovaird's case and ours are also similar, but our case is the first one in which the bone-marrow was examined and the endothelial hyperplasia discovered.

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## SUCTORIAL AND OTHER INSECTS AS PLAGUE CARRIERS.

## A NEW SPECIES OF RAT FLEA.

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AMONG over twenty fatal plague cases investigated by the writer there was one in which it strongly appeared that the infecting bacilli had been carried into the body of the patient—a child—by *pediculi capitis*. It is stated advisedly that this mode of infection appeared very probable, because it is naturally impossible to be certain beyond doubt as to such an occurrence. Only experimental trials on human beings could firmly establish the possibility of this mode of transmittal; but such tests with plague bacilli are of course, inadmissible.

The question whether insects, and particularly parasitic ones, play a more or less important role in the spreading of plague is still far from being settled definitely, as the views of investigators and writers upon this subject are much divided. Among the modern workers on plague who first gave their attention to insects as plague carriers is Hankin,<sup>1</sup> who reports that he carried out a long series of researches on the relation of rat-cadaver-eating ants to the possible spread of plague. He found that ants neither die of plague nor retain the infection for any time. By making extracts of ants shortly after they had eaten from rats dead of plague, Hankin obtained a material which, when injected into rats and mice, would kill them, producing typical plague lesions in them.

Ogata,<sup>2</sup> in studying a plague epidemic in Formosa, took seven fleas from a rat dead of plague, crushed them between sterile slides,

and injected the material so obtained into two mice. One of the latter died of plague, while the other one remained well.

La Bonadiere and Xanthopolides<sup>3</sup> showed, as they maintain, by cultural methods the presence of plague bacilli in a mosquito (moustique) which had bitten a patient sick with plague.

Simond<sup>4</sup> is inclined to attribute much importance to rat fleas as plague carriers. He found bacilli similar morphologically to that of plague in fleas taken from rats affected with the disease. He inoculated three mice with material obtained from such fleas, but only one of them died, the other two surviving.

Loir<sup>5</sup> goes so far as to see in the flea the principal intermediary carrier of plague between rat and man; but, as Galli-Valerio has pointed out, Loir has really no valid experiments to support his claim, which he, however, sees fit to bring forward as a demonstrated fact.

Kolle<sup>6</sup> has systematically tried to infect healthy rats from those sick with or dead of plague through the agency of fleas. He has, however, never succeeded in transmitting plague in this manner, though he was able to demonstrate that fleas had really travelled from sick rats to healthy ones. From his observations on rats he thinks that the disease spreads among these animals owing to the habit of the living to eat the cadavers of the dead of their own kind, and not through the agency of fleas passing from plague-sick to healthy individuals. The primary bubo in rats dead from plague is generally found in the submaxillary region, which points to an infection through a slight lesion in the buccal mucosa. Kolle, in speaking on the subject, very properly remarks: "It is clear that plague bacilli will enter the body of parasitic insects which suck the blood of animals sick with plague. It has, however, not yet been shown beyond a doubt that the bite of such parasites will infect other healthy animals."

Nuttall<sup>7</sup> made experiments to clear up the question as to what part insects play in the spread of plague. He demonstrated that when flies had been fed on material containing plague bacilli they still harbored the virulent organisms twenty-four and forty-eight hours after the last feeding. According to this author, the danger of a spread of the disease through bed-bugs is very negligible. The evidence in favor of the "flea hypothesis" as far as the spread of plague is concerned, Nuttall<sup>7</sup> considers worthless and unable to withstand scientific criticism. He states that all of his attempts to infect rats or mice through the bites of freshly infected fleas have proved futile.

Galli-Valerio<sup>8, 9, 10</sup> severely and justly criticises the evidence so far brought forward to show that rat fleas play the most important role in the dissemination of plague among the human inhabitants of a district infected with this disease. He particularly shows that most of those who have on very insufficient evidence assumed that

fleas from rats spread plague among human beings have not even ascertained whether the species of fleas infesting the rats will at all bite man. Galli-Valerio found *typhlopsylla musculi* and *pulex fasciatus* on European rats and mice under normal conditions. He allowed himself to be invaded by fasting individuals of these two flea species, but neither of them bit him. *Pulex serraticcps*, the flea infesting dogs and cats, and which occasionally bites man, was not found by Galli-Valerio on rats.

Tidswell,<sup>11</sup> who made his observations during the last plague epidemic at Sydney, reports that he collected one hundred fleas from rats, of which ten were identified as *pulex fasciatus*, eight as *typhlopsylla musculi*, one as *pulex serraticcps*, and eighty-one as *pulex pallidus*. The last one, it appears, has not previously been mentioned as occurring on ordinary rats; its stated hosts are, according to Thompson, *mus albipes* of Socotra, and *herpestes ichneumon* of Egypt. This species, the author states, bit human beings in laboratory trials, as did also *pulex fasciatus* on one occasion. *Typhlopsylla musculi* did not bite.\*

Thompson,<sup>12</sup> who during the Sydney epidemic observed blebs which he considered to be produced by fleas and to be the place of entrance of the plague virus, concludes that the transmission of plague from rats and mice through the intermediation of fleas must be very frequent.

Zirolia<sup>13</sup> believes that plague can be easily spread by fleas. He observed *pulex irritans* and *pulex serraticcps*, after they had been fasting for some time, suck blood from a plague-infected mouse, and he found living, virulent plague bacilli in the body of the fleas from seven to eight days after they had partaken of the infected blood. Zirolia also says that the feces of fleas from plague-infected animals contain virulent bacilli and that these parasites survive for a long time in the bodies of dead fleas.

Maxwell,<sup>14</sup> from his observations made in Changpoo, China, states that he is getting to be more and more doubtful about the rat-flea theory. "I cannot see," he says, "how we can escape plague. I must have been bitten in spite of flea powder many times off plague patients, and so must my students. The Chinese, especially the women, catch the fleas and kill them with their teeth. If they catch fleas with plague bacilli in them, how do they escape?"

The Indian Plague Commission,<sup>15</sup> which studied plague in all of its phases in India, has also looked into the question of insects as carriers of the disease, and in its report says that Simond's endeavors to establish the proposition that suctorial insects play

\* Galli-Valerio, trying to invalidate Tidswell's observations, says that this author, like others, failed to transmit plague from rat to rat through the agency of fleas, and proposes the question: "If the transmission is so difficult from rat to rat, why, on the other hand, should it be so frequent from rats and mice to man who is not, as a general rule, attacked by mouse and rat-fleas?"

an important part in the transfer of plague from sick to healthy animals is so weak as hardly to deserve consideration. The experience of plague hospitals in India, and especially that of the Arthur Road Hospital at Bombay, seems to indicate very clearly that suctorial insects do not come into consideration in connection with the spread of plague. The staff and attendants in the Arthur Road Hospital (where thousands of plague cases are treated) were continually bitten by insects, especially mosquitoes, and yet no cases of transfer of the infection from the sick to the healthy came under observation.

The Commission also states that, on reviewing all the facts which have come to its knowledge, it has little reason to suppose that ordinary, casual contact with plague-infected rats, dead or alive, is especially liable to convey the disease. On the other hand, examples are known of cases where the bite of plague-infected rats and other animals has conveyed the disease.

The report of the Commission, however, does contain some information which suggests that *pediculi* may be factors in the spread of plague. According to the Bombay\* statistics of the plague epidemic of 1896, the rate of mortality per 1000 individuals among the Jains of that city as compared with the rate of mortality among the other castes in its population is surprisingly large, and it is believed to be due to the fact that animal life is sacred among the Jains. "They will not," the report says, "sweep their staircases, or sweep their sleeping-rooms, or their cooking-rooms very often, lest they should destroy some animal life, so scrupulous are they. . . . Not that their places are very dirty. They are a wealthy people, and their places look comparatively clean. . . . The Jains, owing to their aversion to taking life, are said to be infected with parasites."

**A NEW SPECIES OF RAT FLEA.** There has certainly not yet been presented much evidence in favor of the theory that the most important intermediaries in spreading plague from rats to man are fleas from plague-infected rats. Even if rat fleas should have played an important rôle in the spread of plague in Sydney, as maintained by Tidswell and Thompson, their conclusions cannot be generalized. How necessary it is to look into this question in every place where plague occurs endemically or epidemically is shown by our observations made with reference to rat fleas in Manila. Looking into this subject we found, somewhat to our surprise, that the fleas infesting rats in Manila are not identical with those which have been described for other countries. Indeed, the species found here on rats appears to be one which has not yet been described. Previous to the time when the writer began to collect rat fleas, Dr. W. B. Wherry had already secured eight, which he kindly placed at

\* Average mortality per 1000 males in the plague epidemic of 1896 at Bombay, 2.63; per 1000 females, 1.88; per 100 male Jains, 8.69; per 1000 female Jains, 6.77.



my disposal. Thirty-four more were subsequently caught. It is not easy to procure a large number of rat fleas, because, when the rodents have been caught in traps it is found that by the time they are killed and examined the fleas have left them. For this reason Dr. Wherry succeeded in obtaining eight fleas only from fifty-three rats, while thirty-four more were subsequently obtained from about one hundred rats. A few of the parasites were procured alive, were kept in a glass vessel for some time, and were then given a chance to bite both Caucasians and native Filipinos. In not a single instance did any of these fleas bite human beings. We have also collected from persons working in the laboratory, where numerous animals are kept and where a large number of rats are sent for examination for plague infection, a number of fleas which proved to be *pulex irritans* and *pulex serraticeps*. The flea occurring on rats in Manila was never found on human beings.

For most of the following descriptions of the flea found on rats in Manila I am indebted to Mr. W. Schultze, assistant entomologist, Biological Laboratory.

*Pulex philippinensis*, nov. spec., Manila, July 19, 1904. Head, with some very small bristles; front of head high and rounded; eyes round. Above the latter and directed backward are the antennæ, which are club-shaped and consist of three segments. First and third segment equal in size; the third segment cup-shaped; the second segment very small. Superior maxilla elongated, triangular. Palpi maxillarum consist of four segments, of which the last is the longest. The posterior margins of the thoracic segments possess each a row of fine bristles, as do also the abdominal segments. On the latter the bristles extend from the back downward to the middle of the abdomen and from below upward. On the back, on the posterior margin of the eighth abdominal segment are two large bristles. In the male below the external genitals two large bristles on each side—*i. e.*, four in all. Abdomen of the male bent upward. In the interior of its abdomen are the spirally curved internal sexual organs, more or less distinct in different individuals. The abdomen of the female is oval and egg-shaped; on the ninth segment around the external genitals, bristles. In the abdomen of the female between the seventh and the eighth segment is an intestine or sausage-like curved organ, the ovary. Behind it in one individual are several barrel-shaped ova.

The longest bristles are found at the lower ends of the femora. They measure 0.2 mm. in the female, and 0.15 mm. in the male.

Color: Light reddish-brown.

Size of the female: Length, 1.8 mm. to 2.67 mm.; breadth, 0.80 mm. to 1.25 mm.

Size of the male: Length, 1.16 mm. to 1.78 mm.; breadth, 0.70 mm. to 0.75 mm.

Size of the ova: Length, 70 microns; thickness, 55 microns.

*Types in the Collection of the Entomological Division of the Biological Laboratory, Bureau of Government Laboratories, Manila, P. I.*

*Pulex philippinensis* appears to be a stationary parasite of the rat. Found in Manila. It is much like *pulex anomalus*, recently described by Baker,<sup>10</sup> and found by him in California. However, the head, eyes, antennæ, palpi, and bristles offer marked points of differentiation.

It is of interest here to mention that Baker, in his monograph on *American Siphonaptera*, describes a new species of rat flea from Brazil, South America. It is a very large species, the male being 3.5 mm. and the female 5.5 mm. in length. Evidently there are quite a few different species of rat fleas in different parts of the world.

EXPERIMENTS WITH FLIES. Experiments which have been made to demonstrate that plague may be spread by flies are all inconclusive, because the arrangements were such that the transmission of the disease was inevitable. Flies were fed with bouillon containing plague bacilli, and, after varying intervals of time had elapsed, were ground up. The emulsion so obtained was subsequently injected into guinea-pigs or rats, which, of course, died of the disease. Such experiments are inconclusive as far as the possibility of the spreading of plague by flies is concerned.

Experiments were, therefore, so conducted as to imitate more closely what might take place in nature. The organs of plague cases, both from men and from guinea-pigs, were kept in an anatomical glass jar, over which was placed a fly-trap containing a number of flies. The door of the trap was then opened and the flies allowed to come in contact with the plague organs in the lower vessel. After being allowed to remain in the lower vessel for varying periods of time (from one to several hours) they were caused to go up into the trap again by surrounding the lower vessel with some dark material, which made them seek the upper light space. The trap was then closed and placed over an especially constructed fly-proof cage in which had been placed two guinea-pigs. The door of the trap was opened so that the flies could enter the cage. The guinea-pigs had been shaved over an extensive area of the back, and some syrup had been dropped on a few spots, to attract the flies and to cause them to come in contact with the bodies of the animals. This experiment was performed twice, but in neither case did the guinea-pigs contract plague. It had been proved by preliminary trials that the flies which had been allowed to come in contact with and to eat from the organs of plague cases had either in or on their bodies plague bacilli. Flies that had been allowed to come in contact with the plague organs were then caught in a trap, chloroformed, picked up with sterile forceps, and dropped into

slightly alkaline bouillon. In every case the insects gave rise to plague cultures in the media in which they were placed.

Another observation, which was not made experimentally but under perfectly natural conditions, may here be recorded. The San Lazaro Morgue at Manila, a building so constructed as to be insect-proof, owing to the inclemency of the weather, soon got into such a shape that flies could readily go in and out in large numbers. During post-mortem examinations on plague cases flies generally passed freely from the dissected cadavers to those making the examination as well as to others present, and undoubtedly also to persons outside of the building, yet no cases of plague have occurred in the part of the city where the morgue is situated. Hence, no case can be attributed to flies as carriers of the infection.

FIG. 1.



*Pulex philippinensis*, nov. spec. The flea found on rats in Manila. Male.

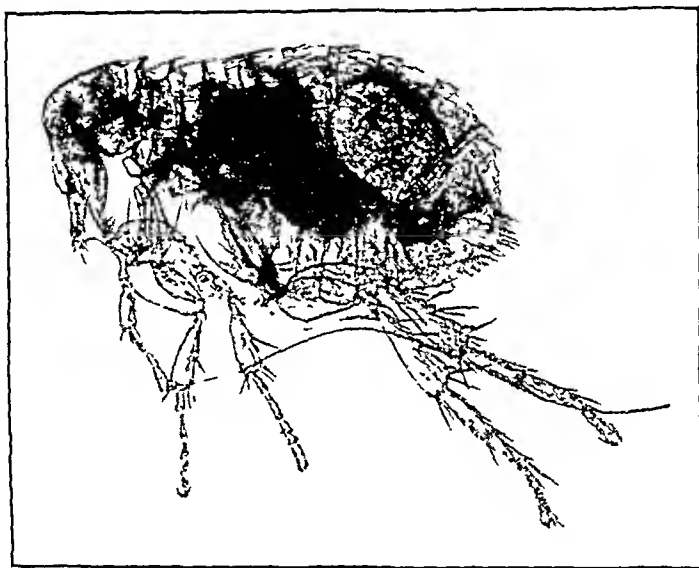
When taking into consideration what has been said above, one is certainly inclined to conclude that insects, as a rule, do probably not play a very important role in the spread of plague. However, that certain parasites may be operative in its transmission is suggested by the observation that this disease is exceedingly prevalent among that caste in Bombay which is probably more infected with pediculi than any other. As stated in the beginning of this paper, a case observed by the writer strongly suggests that pediculi may be carriers of the infection.

*A Case of Bubonic Plague in a Child in which the Injection was Possibly Carried by Pediculi.* The case in question presented the following findings:

Necropsy No. 910, San Lazaro Morgue, Manila, Saturday, March 5, 1904, 4 P.M. Five hours post-mortem. A girl, aged nine years, residing during life in Anda Street, Intramuros, Manila.

The body of a female child, nine to ten years old, well developed. Post-mortem rigidity strong. Post-mortem lividity well marked and extending over the sides of the body, being particularly noticeable around the neck. The cervical glands on both sides are swollen, imparting a doughy sensation to the touch. The tissues in the neighborhood of the swollen glands are quite oedematous. The integument of the body shows no lesions. There is no discharge from the ears; nor does the external meatus on either side show any ulceration. The mucous membrane of the buccal and nasal cavities

FIG. 2.



The same. Female.

are congested, otherwise normal. The scalp is infected with numerous pediculi, which seem to be ill at ease and run about disturbedly. On section of the body the superficial veins discharge a moderate amount of fluid, very dark blood.

The heart is normal, except that the superficial, subpericardial veins are much injected. The myocardium is somewhat soft, dull, and rather pale, pinkish-yellow in color.

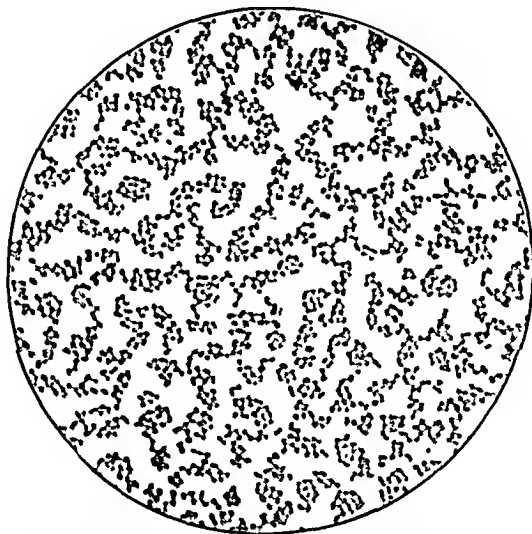
The lungs are pinkish-purple. The lower lobes on the cut surface are dark, reddish-brown, containing much dark, fluid blood, and little air. Some of the areas seen on section are almost in a condition of red hepatization, containing a very large amount of dark, fluid blood. The mucous membranes of the bronchi are slightly swollen, hyperæmic, and moist.

The tracheal mucosa shows the same condition. The larynx is much injected, particularly the epiglottis. The bronchial glands are dark, purplish, slightly swollen, and somewhat softened.

The spleen is of medium size. The capsule is grayish-blue, and smooth as a whole, though slightly wrinkled. The cut surface is reddish-brown. The *trabeculae* are well marked. The *Malpighian* bodies are fairly well visible. The mesenteric glands are reddish-purple, swollen, and rather soft.

Both the kidneys show fairly numerous subcapsular hemorrhagic areas, varying in diameter from about  $\frac{1}{2}$  cm. to a mere point. The capsules peel off easily, and after their removal the surfaces show alternating areas, either deeply injected or grayish-yellow. On

FIG. 3.



Cover-glass preparation of twenty-four-hour-old agar culture of the plague bacillus derived from pediculi. Oil-immersion magnification.

section the vessels appear highly congested, and the glomeruli stand out as deep, reddish-gray points. The tubules are grayish-yellow; the pyramids are deeply injected. The mucous membrane of the pelvis is smooth and slightly swollen, but not hemorrhagic. The substance of the kidneys is soft and almost gelatinous. The suprarenals are large, swollen, congested, and very soft.

The surface of the liver is bluish-pink, mottled with pale, grayish-yellow areas. The capsule is smooth. The cut surface is grayish, pinkish-yellow. The veins contain a good deal of dark, fluid blood. The gall-bladder contains a turbid, yellowish bile; its mucous membrane is smooth.

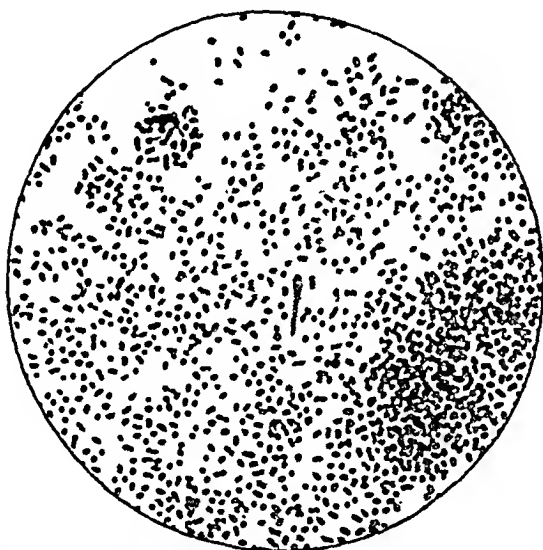
The serosa of the stomach and intestines is injected. The superficial veins are marked as reddish lines. The mucosa, as a whole,

is moderately injected, with punctiform hemorrhages in the ventricular mucosa. The intestinal lymph follicles are somewhat swollen. The peritoneal covering of the uterus and tubes is much injected. All of the fine superficial vessels are visible in consequence of the marked congestion.

The cervical glands on both sides, including those along the sternocleidomastoids and the deeper submental ones, are enlarged, highly congested, and softened. On section a good deal of dark, bloody juice can be scraped from the surface. The smears made from the gland juice show numerous typical plague bacilli.

*Anatomical Diagnosis.* Hemorrhagic, acute, parenchymatous nephritis. Congestion and oedema of the lungs. Moderate fatty degeneration of the liver. Hemorrhagic inflammation. Hyper-

FIG. 4.



Cover-glass preparation of a sixteen-days-old glycerin-agar culture of plague bacilli.  
Involution forms Magnification same as above.

trophy and softening of the cervical glands on both sides. A more or less general hypertrophy of most of the lymph glands. Bubonic plague.

Pieces from the liver, both kidneys, and the cervical glands were placed in Zenker's fluid during the post-mortem examination.

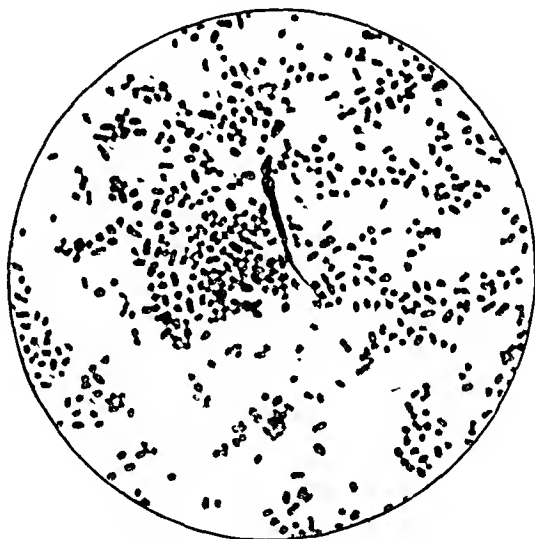
Before the body had been opened three pediculi were picked from the scalp with sterile forceps and dropped into empty sterile test-tubes and later into three flasks, each containing 50 c.c. of sterile, slightly alkaline bouillon. All of the three flasks developed cultures of plague bacilli. The cultures were then transferred to various media, and the bacteria were fully identified as typical plague bacilli. One culture from the spleen and two from the cervical glands likewise developed plague bacilli.

Since this child, dead from bubonic plague, had come from a district which had been considered plague-free for some time, inquiries were made as to the possibility of the girl having been infected with pediculi from some one living in an infected district.

Dr. R. E. S. Newberne, District Medical Inspector, reported on the matter as follows:

"So far as the records show only two cases of bubonic plague, prior to the one under discussion, have occurred on Calle Anda, the first in 1900 at No. 11, and the second in 1901 at No. 137. These numbers being a considerable distance from No. 89 and in opposite directions, it may be assumed that the district is not infected.

FIG. 5.



Same as Fig. 4. Spermatozoa-like involution forms.

"The orphan was taken to 89 Anda Street from the Hospicio de San Juan, December 24, 1903, and remained in good health until the last days of February, when she became ill, complaining of earache and fever, which did not yield to local treatment. The patient was sent to San Juan de Dios Hospital about March 4th, where she died twenty-four hours later, after an illness of nine days.

"So far as can be ascertained, this child did not handle rats or do anything else to which the infection could be ascribed. She slept on a petate on the floor of one of the upstairs rooms, as is the custom of Filipino children.

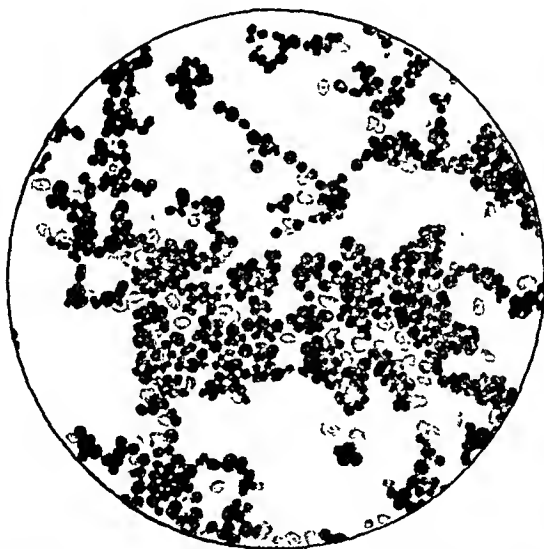
"With the exception of the time—from February 7th to 16th—when she attended the public school, she did not associate with children outside of her home. The family assert that she was free from vermin when she was sent to the hospital, though it was admitted that Filipino children are generally infected with *ped-*

*iculi capitis*. Five bed-bugs, found in the crack of the floor upon which she slept, have been sent to the laboratory; also thirteen rats were sent."

Mr. Charles B. Hare, assistant bacteriologist in the Biological Laboratory, who examined the rats, did not find any evidence of plague in them. Smears were made from the five crushed bed-bugs, which likewise did not show any plague bacilli. It was intended to test the bed-bugs by cultural methods, but this was overlooked by mistake.

*Histopathology of the Case.* Pieces of tissue from the primary cervical bubo, from both the kidneys and from the liver, were fixed in Zenker's solutions, sectioned and stained by various methods, including Weigert's fibrin stain.

FIG. 6.



Cover-glass-preparation of a three-days-old 4 per cent. salt-agar culture of plague bacilli, showing the yeast-like involution forms. Magnification same as above.

Sections from the cervical glands show, even on superficial examination, a number of most profound changes, namely: 1. Almost complete loss of the normal structure and differentiation of the gland into cortical follicles and medullary cords. 2. Advanced coagulation necrosis. 3. Extensive free-blood extravasation. 4. Deposit of granular and fibrillar fibrin. 5. The presence of enormous solid, irregularly distributed masses of bacteria.

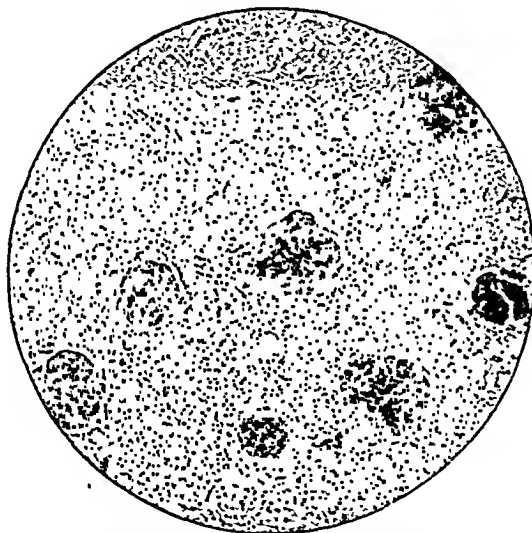
The deeper portions of the cortex still present some oval compartments outlined by fibrous connective tissue, evidently once the trabeculae; the latter, however, do not surround any normal lymph follicles, but masses of necrotic tissue and free extravasated blood. Where the dense masses of bacilli are located there are few tissue elements left. The cells which are still recognizable as such are



mononuclears, and their nuclei generally show a marked pyknotic condition. At the margin of the bacillar masses and clumps there are more normal mononuclear and polynuclear cells, among which are quite a few eosinophiles. Almost as numerous as the latter are plasma mast cells. Bacilli are found also in the tissue next to the large colonies. The bacilli here do not form solid, dense masses, but are freely distributed among the cells. Intimately mixed with the leukocytic cells and the bacilli are numerous red blood corpuscles.

The peripheral tissue, next to the capsule, show a dense infiltration, with completely degenerated erythrocytes and with hæmatoidin and hæmosiderin. This zone apparently is part of the former lymph sinus, which, however, can no longer be distinctly recognized as such. Here, likewise, numerous bacilli are found.

FIG. 7.



Section of kidney in a case of bubonic plague. Stained with Weigert's fibrin stain and showing hyaline thrombi in the glomerular vessels. Zeiss AA Comp. Oc. No. 4.

Fibrin is quite irregularly and extensively distributed throughout the gland. In its interior it is found to be in the form of a granular deposit, and also in the shape of coarser or finer threads. Around the dense masses of bacilli it occurs in the form of a fibrillar network, sending fine threads into masses of micro-organisms.

The tissue next to the capsule—*i. e.*, the former lymph sinus—likewise contains a network of fibrin. The small vessels are more or less completely occluded by hyaline (fibrin) thrombi. These are seen both in the interior of the gland and in the capsular vessels. Here and there the fibrin extends from the interior of a vessel, through its wall into the perivascular tissue.

Few bacilli or none at all are found in the bloodvessels, both in those with open lumina as well as in those where the latter are

occluded by a hyaline thrombus. This condition prevails even in vessels surrounded by innumerable bacilli. The picture clearly furnishes histological evidence that bubonic plague is not primarily a hæmatogenous infection, and that, while the lymphatic infection may be enormous, the blood may still be little invaded by *bacillus pestis*.

The bacteria found so numerous in the sections of the glands show all the morphological characteristics of plague bacilli.

*Kidneys.* The renal tissue presents a most striking picture. Sections from both kidneys, treated by Weigert's fibrin method, look as if the vessels had been injected with a violet-stained gelatin. There is not a normal glomerulus seen anywhere. All the sections show a more or less complete obliteration by hyaline thrombi. In

FIG. 8.



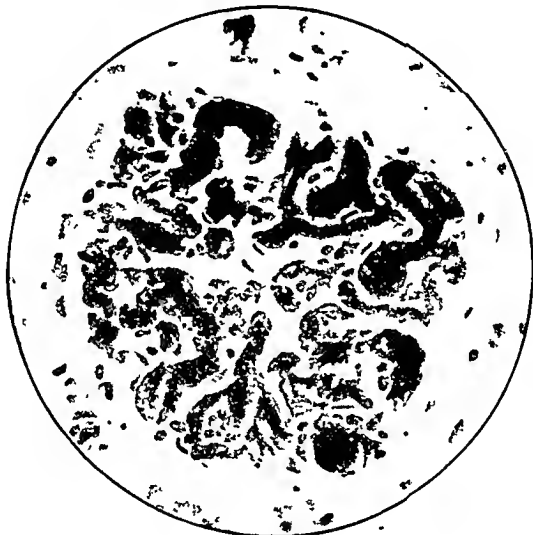
most of the Malpighian bodies the hyaline thrombosis of the capillaries is so perfect that both the main branches of the afferent vessel and the smaller capillaries given off from the larger loops are sharply outlined.

Most of the thrombi appear to be perfectly solid; some, however, exhibit a hollow space in the centre, as can be seen both in transverse and in longitudinal sections.

The endothelial lining of the thrombosed vessels is well preserved. Where the thrombi are comparatively thin one can see, both in longitudinal and in transverse sections, endothelia which are perfectly normal to all intents and purposes. Nowhere do the thrombosed vessels show to any extent a loss of endothelia. The thrombosis can, therefore, not be attributed to a denudation of the vessels of their endothelial lining. L. Loeb<sup>17</sup> a short time ago reported

some experiments on certain conditions of blood coagulation. He concluded that after the removal of the endothelial lining specific enzymes are extracted from the tissues and so act upon the fibrinogen, which is held in colloidal solution, that fibrin is precipitated. Since in our case a loss of endothelia in the thrombosed vessel is not demonstrable, the thrombosis cannot be attributed to such a loss. Perhaps the hypothesis that toxic influences may have so damaged the endothelia that they became permeable to the substances producing coagulation, is justifiable. Such disturbances of the functions of cells by toxic influences without demonstrable morphological changes are, of course, not unknown.

FIG. 9.



The capsules of Bowman are likewise normal, though a few of them show a very moderate amount of thickening; their lining epithelium exhibits no marked changes. In some places the hyaline thrombi are continued into the vasa afferentia and efferentia and even into the vessels of which these are branches. Quite commonly there are seen between the uriniferous tubules parts of such small vessels filled with hyaline thrombi. However, none are found in the larger arteries or veins, in some of which finely granular fibrin and desquamated endothelial cells are present. The vessel walls themselves show no damage aside from the denudation of the intima. There is in particular no extension of the fibrin through the vessel walls, nor is there any evidence of mesophlebitic or periphlebitic or arteritic processes.

The epithelial cells lining the convoluted uriniferous tubules are somewhat swollen, with indistinct outlines and a vacuolated protoplasm, but their nuclei are yet quite normal. A granular material

partly fills some of the convoluted tubules. The epithelial lining of the straight tubules does not show any marked changes. The capsule of the kidney is normal. Nowhere do any of the renal bloodvessels show a large number of plague bacilli, a few of which are possibly seen inside the lumina of bloodvessels; but even this is not certain, being, on the contrary, rather doubtful. A moderate number of bacilli, however, are seen in the lymph clefts between the tubules and around the Malpighian bodies.

The profound vascular change, the complete obliteration of capillaries, small veins and arteries by a homogeneous, hyaline material is apparently due to toxic influences.

A few slender, long bacilli, which keep Gram's stain, are occasionally found in the tubules. They are probably of no significance and represent an agonal or post-mortem invasion.

FIG. 10.



Section of kidney in a case of bubonic plague. Stained with Weigert's fibrin stain and showing hyaline thrombi in glomerular vessels. Oil-immersion magnification.

Welch<sup>18</sup> has reported an observation of complete glomerular, capillary, hyaline thrombosis which is identical with the one described above. In his article on "Thrombosis," in Allbutt's *System of Medicine*, he says: "The most striking example of this form of (hyaline) thrombosis with which I am acquainted is encountered in the renal capillaries, chiefly of the glomeruli, of swine dead of hog-cholera, or of animals infected with the hog-cholera bacillus. In extreme cases there is complete anæmia, and it may be impossible to force more than a minimal amount of injecting fluid into the renal vessels. Sections stained with Weigert's fibrin stain look as if the capillaries had been injected with Berlin blue. Ribbert found similar hyaline thrombi in the kidneys of rabbits inoculated with

*staphylococcus pyogenes aureus*. I have repeatedly found them in various experimental infections and in human infections. They occur in eclampsia. Bacteria are not necessarily present, so that toxins are probably the underlying causative factor, and for this there is experimental evidence."

Hyaline thrombosis of the glomeruli vessels is not a rare occurrence in plague, because we have encountered it seven times in the study of about twenty cases of this disease.

Sections of the liver show a very few small periphlebitic inflammatory foci composed of small, round mononuclears. The liver cells all show a coarse vacuolation, some of the vacuoles being larger than the nuclei. The capillaries are moderately filled. There is no free, extravasated blood. A very few plague bacilli are found between the liver cells.

A study of this case shows it to be one of bubonic plague, with the cervical glands as the seat of the primary bubo. In the absence of all wounds on the head, the neck, the mucosa of the nose, the buccal cavity, etc., and in view of the fact that plague bacilli could be demonstrated in the pediculi, it is perhaps not unreasonable to consider it probable that in this case the infection was conveyed through the bite of pediculi coming from another individual infected with plague.

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## REVIEWS.

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LECTURES TO GENERAL PRACTITIONERS ON THE DISEASES OF THE STOMACH AND INTESTINES. By BOARDMAN REED, M.D. New York: E. B. Treat & Co., 1904.

THE literature of diseases of the stomach and intestines is constantly being enriched to keep pace with recent advances in methods of diagnosis and treatment, and this, the most recent American contribution in the form of a course of lectures delivered by the author to his students, is intended to present "in a single volume the whole subject of diseases of the stomach and intestines from the standpoint of our present knowledge," without professing to enter into profound discussions of the many questions that are still *sub judice*. The lecture style which the author has chosen is more in keeping with direct, at times, perhaps, dogmatic statement, than with academic discussion; yet, although his teaching represents mainly his own views, his attitude is that of a conservative physician, a careful student of other men's ideas and experience in a subject in which a wide divergence of opinion obtains on questions of vital importance to the life and welfare of patients.

In the physical examination of the abdomen the writer recommends the simpler clinical methods which can be carried out without complicated apparatus and without causing the patient discomfort; in ordinary cases he relies chiefly on percussion and the effect of filling the stomach with water (clapotement) to determine position and size, as well as motility of the stomach. Inflation with carbon dioxide, he, in agreement with most other authorities, regards as a useful and perfectly safe procedure, but uses hydrochloric instead of tartaric acid, with bicarbonate of soda to produce the carbon dioxide. The lectures on uranalysis and examination of the feces and blood at least do not err on the side of prolixity; but the part devoted to the feces is disappointing. Writers on gastric and intestinal diseases are fond of dwelling on this subject of the examination of feces and of deploring the lack of interest on the part of the general practitioner; but aside from pathogenic bacteria and possibly the ova of parasites, the findings obtained with the microscope add but little to the information obtained by naked-eye examination, which no careful diagnostician would think of neglecting.

The last lecture in the section devoted to diagnosis is entitled a "Symptomatic Guide to Diagnosis," and contains a list of symptoms, arranged in alphabetical order, with a list of possible causes

in a parallel column opposite. Now, this method of approaching the difficult subject of diagnosis, which imitates the actual conditions that confront the doctor when he sees the patient for the first time, has been successfully employed by certain authors, notably in England, and might with advantage to the student be exploited more generally by systematic writers. But the author has, unfortunately, contented himself with the mere enumeration of individual symptoms on the one hand and etiological factors on the other, which is really no guide at all, as it does not afford the slightest hint to help the bewildered student in arriving at anything like a definite conclusion in a given case. If, instead of individual symptoms, the author had presented a series of clinical syndromes, and if, instead of attempting to give every conceivable etiological factor, he had contented himself with the most probable causal condition, the practical value of this chapter would have been very much greater.

Of the 178 pages devoted to methods of treatment (Part III.), 140 are taken up with methods other than drug-giving, and the remaining 38 with the medicinal therapy of the diseases of the stomach and intestine. A large portion of this space is devoted to dietetics and contains a sufficiency of tabular matter showing food values, the requirements of different classes of individuals, the ingredients contained in different food articles, and the author's progressive series of diets, besides Leube's and Penzoldt's diet schemes, with some sound criticisms of the latter from the American point of view.

As the armamentarium of a specialist in diseases of the stomach is not complete without electrotherapeutic apparatus, so an up-to-date text-book would not be complete without a full description of the various forms of electricity that are now used in the treatment of patients. Among the newest of these methods are the high-frequency and so-called polyphase electric currents. The high-frequency currents, we learn, are most suitable for application within cavities from the fact that they produce practically no sensation. Other special methods, such as Cleaves' hydroelectric treatment within the bowel and the like, are also mentioned, but without critical comment. Whatever kind of electricity is employed, it appears that the effect, with one exception, is constantly the same—in one word, *tonic*—and the conditions that are benefited by electric treatment are, therefore, gastric dilatation, atonic dyspepsia, and, in fact, all atonic conditions. The interesting exception, according to the author, is that with a high-tension coil, which, being practically painless, permits the application of a strong current, the function of the gastric glands can be depressed; that is, hyperchlorhydria is diminished. The author makes extensive use of the intragastric faradic current, for which he has designed an electrode modified from Einhorn. He contends that the procedure is as easy of application as lavage.

Hydrochloric acid stimulates the secretion of the gastric glands and does not inhibit fermentation; it should be combined with pepsin, as a rule, and a smaller dose than that advised by most authorities is recommended: from 4 to 5 drops of the dilute acid after meals up to 10 drops, and, in exceptional cases, 20 or 30 drops in a tumblerful of water, which the patient is directed to sip slowly. His experience must have been rather exceptional on this point, and he appears to regard the drug purely as a stimulant to secretion.

Alkalies in small doses stimulate and in large doses diminish the production of hydrochloric acid, irrespective of the relation between administration and the ingestion of food. The truth about this much-debated question probably is that when the stomach is full and a large portion of the acid has already combined with the food, a smaller dose of the alkali suffices to neutralize the remaining excess of hydrochloric acid; in short, the dose must be adapted to the quantity of acid to be neutralized at the time of administration. With papoid, caroid, and other digestants of the same class, the author's experience appears to have been as disappointing as that of most physicians who have given these substances a thorough trial.

The lecture on the treatment of appendicitis contains a critical review of the different schools, of which there are three, according to our author. The radical surgical school, represented by Deaver, of Philadelphia; Morris, of New York, and Murphy, of Chicago; the conservative school, comprising a large number of prominent surgeons, Keene, Richardson, White, Parke, and a long list of others; and the "surgico-starvation method," advocated by Ochsner. While the author's attitude is impartial and his judgment is based on the results reported by exponents of each of the three methods, it is not difficult to see that he is, if not entirely convinced, at least very strongly impressed by the teaching of Ochsner.

A succinct epitome of the surgery of the stomach and intestines completes the volume, which, considering the generous size of the type and illustrations, has been kept within reasonable limits, while a very good working index makes up for the somewhat unwieldy length of the table of contents.

R. M. G.

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SERUMS, VACCINES, AND TOXINS IN TREATMENT AND DIAGNOSIS.  
By WILLIAM CECIL BOSANQUET, M.A., M.D. Oxon., F.R.C.P.  
London. Chicago: W. T. Keener & Co. London: Cassell &  
Co., Limited, 1904.

DR. BOSANQUET in this small book has collected much information which is both useful and interesting. Instead of an enthusiastic, unscientific plea for the use of these newer remedies, one finds a just treatment of facts in which statistics are given and original author-



ities are quoted. The opening chapters present a short *résumé* of the modern conceptions of immunity developed particularly along the lines of the "side chain" theory of Ehrlich. Then come chapters upon the preparation and administration of serums and vaccines, and the use of serums and toxins in the diagnosis of disease. The major portion of the book, however, deals with the treatment and prevention of various diseases by means of antisera, antitoxins, and vaccines. To all the important affections a separate chapter is devoted. The book is essentially modern, but on account of the very fact that it deals with problems which are in the process of building, its greatest value and interest are for the present alone.

W. T. L.

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ESSENTIALS OF MEDICAL CHEMISTRY, ORGANIC AND INORGANIC, CONTAINING ALSO QUESTIONS OF MEDICAL PHYSICS, CHEMICAL PHILOSOPHY, ANALYTICAL PROCESSES, TOXICOLOGY, ETC. Prepared especially for students of medicine. By LAWRENCE WOLFF, M.D. Sixth edition, thoroughly revised, by A. FERREE WITMER, PH.G. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

SINCE this small book has gone through six editions, there must be a demand for it, though a study of even this last revised edition fails to explain the reason. In the mass of questions and short answers new material may be found here and there. The term "Chemical Philosophy" seems to appear only in the title. The book represents the typical "Quiz Compend."

W. T. L.

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SURGICAL EMERGENCIES: THE SURGERY OF THE ABDOMEN. Part I. Appendicitis and Other Diseases about the Appendix. By BAYARD HOLMES, B.S., M.D., Professor of Surgery in the University of Illinois; Professor of Clinical Surgery in the American Medical Missionary College, Chicago; Attending Surgeon to the Chicago Baptist Hospital. New York: D. Appleton & Co., 1904.

THIS small volume contains a large amount of material. It represents the author's experience in the treatment of appendicitis and some other abdominal diseases, and a careful consideration of the pathology and symptoms of each. One is impressed with the author's earnestness and conviction regarding his views, but at the same time he is open to the criticism of being anything but generous respecting the views of others. A large part of each chapter is taken up with minute reports of cases. His criticism of the Ochsner treatment is unnecessarily severe; he does not, however, attach Ochsner's

name to the treatment. He classifies it with osteopathy and Christian Science. Although we agree with the author that every case of appendicitis should be operated upon, and that medical treatment should be given no place excepting when operation is impossible, we regret the light way in which he speaks of the opinion of recognized authorities. He also shows a tendency to illustrate his remarks by a discussion of his own successes and others' failures. His after-treatment probably shows his individuality more than anything in the book. After a simple removal of the appendix the patient is allowed to walk to his room from the operating-table if a local anæsthetic has been used; to get out of bed on a commode, or sometimes to go to the closet for the purpose of urination or defecation; to sit up in his chair at his meals on the day following operation, and after that is allowed to walk about the hospital. A list of twenty-nine cases operated upon during twelve months is given, in which the time spent in bed varied from five hours to twenty-one days. Thirteen of these patients were out of bed in forty-eight hours or less. The administration of liquid and semiliquid diet in the simple cases is begun within a few hours after the operation. No abdominal support is advised, and no restriction as regards exercise is made. It is stated that the patient should be able to leave the hospital within a week.

The closing portions of the book deal with peritonitis, some of the varieties of intestinal obstruction, perforated typhoid ulcer, and malignant disease of the intestine. The book closes with several pages of adages. The reader is impressed at once with the author's clearness of statement, his absolute conviction in the various positions taken, and especially those in which he differs from a large majority of surgeons.

J. H. G.

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THE SURGERY OF THE HEART AND LUNGS. A History and Résumé of Surgical Conditions found therein, and Experimental and Clinical Research in Man and Lower Animals, with reference to Pneumonotomy, Pneumonectomy, and Bronchotomy, and Cardiotomy and Cardiography. By BENJAMIN MERRILL RICKETTS, Ph.B., M.D., Member of the American Medical Association, Western Surgical and Gynecological Association, International Medical Congress, 1887, etc. New York: The Grafton Press, 1904.

THE advancement which has been made during the past few years in the surgery of the heart is simply remarkable. The medical journals have been full of reports of interesting and unusual cases, especially of stab wounds treated by surgical operation. The subject is one of peculiar interest to all surgeons, and there is naturally a demand for a book devoted to this subject.

The author has contributed largely to the surgery of the heart and lungs, especially the experimental side of the subject, and with his papers many are no doubt familiar. A large part of this book is devoted to history and bibliography, and is consequently made up largely of quotations and references. This portion, therefore, will be found of inestimable value to anyone who wishes to look up the surgery of either the heart or lungs. No attempt has been made on the author's part to consider all the diseases of the heart and lungs, but only those which may require surgical interference. He has been most careful to verify all his statements with references. The original part of the work consists in a report of his extensive experimental work on dogs.

This book is a most valuable contribution, and one for which we bespeak a marked success.

J. H. G.

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A TEXT-BOOK OF CLINICAL DIAGNOSIS BY LABORATORY METHODS. FOR THE USE OF STUDENTS, PRACTITIONERS, AND LABORATORY WORKERS. By L. NAPOLEON BOSTON, A.M., M.D., Associate in Medicine and Director of the Clinical Laboratories, Medico-Chirurgical College, Philadelphia; formerly Bacteriologist at the Philadelphia Hospital and at the Ayer Clinical Laboratory of the Pennsylvania Hospital. With 320 illustrations, many of them in colors. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

BEGINNING with an explanation of the mechanics of the microscope itself, the author has taken pains to be explicit in his account of the various techniques. The opening chapter considers the care and use of the microscope and its accessories, and explains the laws of refraction and the values of the different lenses usually employed. This attention to detail is manifest throughout the book.

In the section on blood there is a complete description of its examination in health and disease, including a study of cryoscopy and osmosis. Later, the different diseases of the blood are taken up, and their special pathology and bacteriology studied seriatim. The author has, unfortunately, not been so systematic in the chapters devoted to the analysis of urine, but has, however, given an exhaustive treatise on that subject.

A very good account of animal parasites is included under the different chapters on the blood, the urine, and feces. The examination of the secretions of the nose, eye, mouth, and the genital organs is taken up in the latter part of the book, as is also the analysis of milk and the study of the parasitic skin diseases.

There are over 300 illustrations, with a number of colored plates, those illustrative of the malarial parasite being especially noteworthy.

With perhaps the exception of the section on the urine, the contents of the volume are remarkably well arranged, and the work will be of considerable value to those to whom the ready access to a modern clinical laboratory is not practical.

A. N.

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A TEXT-BOOK OF HUMAN PHYSIOLOGY. By ALBERT P. BRUBAKER, A.M., M.D., Professor of Physiology and Hygiene in the Jefferson Medical College; Professor of Physiology in the Pennsylvania College of Dental Surgery, etc. With colored plates and 354 illustrations. Philadelphia: P. Plakiston's Son & Co., 1904.

INASMUCH as this book is written for the medical student and practitioner, and is designed particularly to present the more important facts of physiology which have to do with the practical aspect of medicine, much of the technical portion of the subject is omitted, and the normal functions of the various organs and systems are related in an interesting and readable manner. The treatment of the subject is developed along the usual lines, and does not differ especially from other text-books of this nature. The paragraphing is well arranged, so that one can readily refer to any particular subject. One might mention a few instances, as in the discussion upon the origin of leukocytes, or upon the histology of the lymphatics, where the author's statements do not coincide with the current views concerning these subjects, but with a few exceptions the book is generally good.

W. T. L.

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A TEXT-BOOK OF PATHOLOGY. FOR PRACTITIONERS AND STUDENTS. By JOSEPH MCFARLAND, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia; Pathologist to the Philadelphia Hospital, and to the Medico-Chirurgical Hospital, Philadelphia. With 350 illustrations, a number in colors. Philadelphia, New York, and London: W. B. Saunders, & Co., 1904.

THIS work of 818 pages is a systematic treatise on general and special pathology. The ground, as far as the principles of pathology are concerned, is well covered, and the arrangement of the book is good. The subject of general pathology is first discussed. Here the questions of general etiology, defects of development, pathology of nutrition and of the circulation, characteristics of cell life, retrogressive and progressive tissue changes, parasitism, immunity, and infection are taken up. The accepted teachings are usually set down, but the "pros and cons" of the various undecided points are not, as a rule, given.

Under the heading of Special Pathology, the diseases of the various systems and organs are taken up in a well-ordered manner, the degenerations, hypertrophies, infections, etc., of each being discussed. A voluminous index of fifty-four pages adds to the value of the book. The size of the book is, perhaps, a fault, as it contains more than is really needed in teaching the subject to students of medicine, while it hardly covers the field of pathology with enough comprehensiveness to satisfy one as a work of reference.

The author's style is somewhat elaborate in places, and clear conceptions are not at all times given. The book contains some good photographs, while the drawings are of average quality. It presents an attractive appearance.

G. C. R.

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THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Comprising ten volumes on the Year's Progress in Medicine and Surgery, issued monthly. Under the general editorial charge of GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Post-graduate Medical School. Vol. IX. Physiology, Pathology, Bacteriology, Anatomy. Dictionary edited by W. A. EVANS, M.S., M.D.; ADOLPH GERHMANN, M.D., and WILLIAM HEALEY, A.B., M.D. Chicago: The Year Book Publishers, 1904.

THIS number preserves the same general form and arrangement as the preceding ones. The reviews are, as usual, quite full and comprehensive, while much of the important work of the year, particularly that possessing practical interest, is touched upon. The majority of the references, however, are confined to English and American authors.

It is very unfortunate that, evidently in binding, a portion of the authors' index should have been omitted.

W. T. L.

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A TEXT-BOOK OF PHYSIOLOGICAL CHEMISTRY. FOR STUDENTS OF MEDICINE AND PHYSICIANS. By CHARLES E. SIMON, M.D. Second edition, revised and enlarged. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS second and enlarged edition of Dr. Simon's book should be particularly appreciated just at this time, for of late the extensive and important researches in physiological chemistry have rendered much service to medicine in general. Use has been made of these recent contributions and there is evidence of much revision. Particularly noteworthy are the chapters on Albumins, on the Products of Nitrogenous Katabolism, and on Gastric and Tryptic Digestion. Though the book is "intended as a text-book for the lecture-room

and as a guide in the physiological-chemical laboratory," many of the chapters may be read with great interest away from the laboratory. At the same time there is an appendix of laboratory exercises which serves as a guide to the student in performing certain experiments. The book should prove to be very useful. W. T. L.

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A PRACTICAL TREATISE ON DISEASES OF THE SKIN. FOR THE USE OF STUDENTS AND PRACTITIONERS. By JAMES NEVINS HYDE, A.M., M.D., Professor of Skin, Genito-urinary, and Venereal Diseases, Rush Medical College, Chicago, etc., and FRANK HUGH MONTGOMERY, M.D., Associate Professor of Skin, Genito-urinary, and Venereal Diseases, Rush Medical College, Chicago, etc. Seventh and revised edition, illustrated with 107 engravings and 34 plates in color and monochrome. Philadelphia and New York: Lea Brothers & Co., 1904.

THIS well-known treatise upon diseases of the skin has again been subjected to an extensive and thorough revision by its authors. In addition to a considerable number of new sections descriptive of diseases not considered in previous editions, much new material has been added to the old sections, many of which have been entirely or in large part rewritten. So far as we have observed, nothing of any real importance among the recent acquisitions to our knowledge of diseases of the skin has been overlooked.

Among the most interesting and important of the new sections introduced are those devoted to the consideration of radiotherapy and phototherapy. The  $x$ -ray and light bid fair to take rank among the most important additions for many years to the armamentarium of the dermatologist, and the indications for the employment of these powerful agents in diseases of the skin and the method of using them are treated in a manner commensurate with the importance of the subject.

Under the title "Psoriasiform Dermatoses," a group of affections is described whose members have been reported in the past fifteen years under a great variety of names by different observers. Brocq, who has recently written at some length upon this group, has proposed to name it *parapsoriasis*; as this seems to us a fairly unobjectionable designation, we think the authors, instead of adding to the huge burden of names under which dermatology has so long groaned, might well have adopted it.

We note that the section which in former editions appeared under the title "Dermatoses of Scrofulous Subjects" is now called "Dermatoses Probably Tubercular," an unmistakable indication of the marked change which has taken place in the manner of viewing this most important group of diseases.

The value of the book has been much enhanced for workers in

this branch of medicine by the great increase in the number of references to the literature of dermatology.

This new edition will easily take rank among the three or four best books upon cutaneous diseases. It is a clear and comprehensive exposition of the most modern views upon the subject, and we heartily recommend it to those who wish to have the latest word upon diseases of the skin.

M. B. H.

THE STUDENT'S HANDBOOK OF SURGICAL OPERATIONS. By SIR FREDERICK TREVES, Bart., K.C.V.O., C.B., LL.D., F.R.C.S., Sergeant Surgeon-in-Ordinary to H. M. the King; Surgeon-in-Ordinary to H. R. H. the Prince of Wales; Consulting Surgeon to the London Hospital. New edition, revised by the author and JONATHAN HUTCHINSON, Jun., F.R.C.S., Surgeon to the London Hospital; Examiner in Surgery, Royal Army Medical Department. (Abridged from the author's *Manual of Operative Surgery*.) Chicago: W. T. Keener & Co., 1904.

THE present volume is a condensation of the author's more extensive work, which is so well known to the profession. For a book of its size it contains a wonderful amount of information and is excellently illustrated. It can be heartily commended for the use of students. The arrangement is the same as in the larger work, and the most essential features of the various operations are emphasized. It differs from the larger work in that the general principles of operative surgery and a consideration of the value of the various methods are not discussed. The anatomy of the various parts, the treatment after operations, the mortality, and the results are also omitted.

J. H. G.

THE UTERO-OVARIAN ARTERY, OR THE GENITAL VASCULAR CIRCLE. Anatomy and Physiology, with Their Application in Diagnosis and Surgical Intervention. By BYRON ROBINSON, B.S., M.D. Chicago: E. H. Colegrove, 1903.

THE description given by the author of the utero-ovarian artery, or, as he calls it, the genital vascular circle, is very complete. The illustrations are very numerous, but many of them might be omitted, because of their great similarity to others. It is evident that the author has expended a great deal of time and effort in the preparation of this work.

J. H. G.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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The Significance of Pulmonary Infusions in the Diagnosis and Therapy of Pulmonary Tuberculosis.—P. JACOBS (*Deut. med. Woch.*, 1904, xxx. 945) says that on guinea-pigs he was able to show that large quantities (5 to 15 c.c.) of fluid could be injected directly into the lung through a catheter passed into the large bronchi without producing any apparent distress to the animals and without being followed by any untoward symptoms. By using various substances (aniline blue, salicylic acid) it was demonstrated that the fluid was thoroughly distributed throughout the lung, that the substances were well borne, and that they were retained for a relatively long time in the pulmonary tissue. If drugs can exert any local effect upon tuberculous processes this direct method of application offers many evident advantages over their administration by mouth or subcutaneously. Together with Bougart the process was tried upon tuberculous cattle, various substances being employed. The five cows used in the experiment received repeated injections of 500 c.c. of fluid during the six months of observation, an average of twenty-five injections per cow, always stood the operation well, and showed no ill effects from the numerous infusions. The fluid was introduced through a soft rubber catheter passed through a tracheotomy tube. The medicaments used were hetol, creosote, tuberculin, methylene blue, and pyoktanin. As a general result, it may be stated that the four cows killed at the end of six months showed improvement, two of them even marked improvement; but in the one treated with pyoktanin the course of the disease was uninfluenced and the animal succumbed. Tuberculin was found to be the most efficacious remedy, then creosote, hetol, and methylene blue in the order named. Anatomically the lungs from the cows treated with tuberculin and creosote showed a definite process tending toward arrest and healing. Together with Dr. Rosenburg the method was then tried on human patients, a soft rubber catheter being passed into the trachea through the larynx. The technical difficulties were soon overcome, and the infusions, as in animals, were well borne. Five cases were treated,



and Jacobs feels justified in concluding that the method is harmless and the therapeutic results encouraging. As an important accessory contribution, he believes the infusion is of great value as a diagnostic procedure. In the presence of pulmonary tuberculosis the patients react to one-tenth or one-twelfth of the dose of tuberculin necessary for a rise of temperature by subcutaneous injection, whereas if the tuberculous lesion be elsewhere in the body it requires the same or even a higher dose by infusion than by subcutaneous injection.

**Arteriosclerotic Abdominal Pain.**—MAX BUCH (*St. Petersburg Med. Wchnschr.*, 1904, vol. 29, No. 27, p. 298). On the basis of an analysis of 25 cases—collected from the literature and from his own observations—Buch draws a clinical picture which he considers distinctive of sclerosis of the vessels in the splanchnic area. The significance of this symptom-complex is an acquisition of the past few years and is a valuable addition to our knowledge of the manifestations of arteriosclerosis in other regions of the body, the sclerosed coronary arteries, arch of the aorta, cerebral, renal, and femoral vessels giving rise to definite and easily appreciated features. The essential mark of all the cases is abdominal pain, but on account of certain secondary features he divides them into two classes. In the first class the abdominal symptoms dominate the picture. The patients, usually over forty years of age, are seized with severe attacks of abdominal pain lasting from a few minutes to an hour and situated almost always above the navel. The attacks recur frequently, often many times a day, and are precipitated by the same factors which are of such importance in the occurrence of paroxysms of angina pectoris, bodily exertion, emotional disturbances, and assuming the horizontal position. In some of the cases attacks of stenocardia occur between the attacks of abdominal pain. In most of the cases there are the evident signs of arteriosclerosis in other regions. The abdominal aorta is seldom enlarged or misplaced, but is constantly tender, the sensitiveness being more marked during the paroxysms. In the experience of Buch all the cases yield rapidly to diuretin or strophanthin, and he sees in this a valuable therapeutic means to test a doubtful diagnosis.

In the second class of cases the epigastralgia is associated with true angina pectoris or anginoid attacks. This group of cases has long been recognized and is well described by Huchard and V. Schrötter. The epigastric pain may initiate the attack or be referred to merely as a radiation of the thoracic pain.

As a rule there are no digestive disturbances in any of the cases and the ingestion of food bears no other relation to the attacks than that too full a meal may precipitate them. Only exceptionally is there meteorism. It must be remarked that there may be, as in other parts of the body, extensive sclerosis of the abdominal vessels without any symptoms. Buch reviews at length the probable causes of the pain.

**A Contribution to the Study of Hemorrhage from Apparently Normal Kidneys.**—HUGO SCHÜLLER (*Wiener klin Wochenschr.*, 1904, xvii. p. 477) reports a case of unaccountable renal hemorrhage in a woman, aged forty-nine years. The onset occurred during a menstrual period, and was associated with fever, vomiting, and headache, which lasted for a day. The hemorrhage, which at first lasted for three months,

was at one time so extensive as to produce marked anæmia, which confined the patient to bed for a month. Six months after onset the right kidney, from which the blood was found to come, was opened on operation by the usual autopsy incision. No gross lesions were found. An examination of a bit of excised kidney showed, however, evidence of an old inflammatory process—*i. e.*, “the presence of small cysts, some containing a colloid material. Occasionally a hyaline cast is found in the straight tubules, but they are more numerous in sections from the regions of the pyramids. The casts stain so deeply and the epithelial cells about them appear so flattened that one may conclude they have been lodged there a long while. In places red blood corpuscles are seen in the straight tubules. In the protoplasm of many of the cells lining the collecting tubules are seen brownish particles of pigment.”

Schüller reviews the literature of cases similar to this, and accepts only two in which careful examination of the excised kidney failed to reveal any pathological affection. He thinks it is better to refer to these two cases as “unexplained” rather than to draw from them the general conclusion that hemorrhage may occur from a perfectly healthy kidney. The varied pathological findings in other cases he groups under seven headings. Congenital malformations, diffuse unilateral nephritis, diffuse or circumscribed unilateral nephritis, glomerulonephritis, fibroid degeneration of the capsula adiposa, mechanical lesions and their effects, and, lastly, a special group for the case described by Abbé, apparently due to calcareous incrustations in a papilla. The purely vasomotor theory advanced by Klemperer to explain the hemorrhage he receives with little favor, and inclines to the view of Albarran, that no matter what role the nervous system may play careful examination will practically always reveal some organic lesion however insignificant. He does not think that we can disregard this lesion on the assumption that it is altogether out of proportion to the clinical manifestations. The exact mechanism of the hemorrhage in these cases remains unexplained.

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**The Leishman-Donovan Body and Tropical Splenomegaly.**—In November, 1900, LEISHMAN observed at the Royal Victoria Hospital, Netley, some curious bodies in smears from the spleens of individuals, who had been invalided home suffering from “Dum-dum” fever. His description did not appear until May, 1903 (*British Medical Journal*, May 30, 1903, vol. i. p. 1252). The name “Dum-dum” was applied to this tropical fever owing to its having extensively prevailed in a cantonment in India of that name. Nearly all the literature on these parasites has appeared in the *British Medical Journal* for the remainder of 1903 and up to the present date in 1904. Donovan’s name is associated with these bodies owing to the fact that he was the first after Leishman to find them in the smears from the spleen in tropical cachexia. He was the first also to find them in the blood smears from the spleen obtained by splenic puncture *intra vitam*. At the recent meeting of the British Medical Association (*British Medical Journal*, September 17, 1904, pp. 642-658) the relationship of these new bodies to tropical splenomegaly and cachexia was thoroughly discussed in the Section on Tropical Diseases.

Briefly stated, the Leishman-Donovan bodies are demonstrable by

the Romanowsky stain or some of its modifications. They are small oval bodies 3 to  $8\mu$  in diameter. Each possesses two nuclei, one much larger than the other and oval in outline. The small nucleus is in the form of a small rod set perpendicularly or at a tangent to the larger one. The protoplasm of the body stains a reddish tint. They usually occur singly or in twos, but occasionally they are grouped together to the number of twenty, embedded in a matrix. It is now conceded that this grouping is due to their being contained within the bodies of macrophages. The bodies are not contained within the red corpuscles, although Laveran holds that they are. There is no authentic evidence of their having been found in the peripheral circulating blood. They have now been observed in a very large number of cases of tropical cachexia and splenomegaly in the splenic blood obtained *intra vitam*.

Clinically the cases present the following symptoms: Irregular remittent or intermittent type of fever; grave anæmia of the secondary type; marked cachexia; progressive emaciation; and great enlargement of the spleen. Occasionally there is a history of dysentery. Most of the cases had previously been regarded as malarial in origin. What is of great interest is the fact that Bentley has shown that the disease known as "kala-azar," of Assam, presenting in general the symptoms enumerated above, is due to infection with this parasite. Homer Wright and others have demonstrated that the disease known as "Delhi boil" is caused by the same organism. It has been shown that the disease produced by the organism is widely distributed. It has been found in various parts of India, and has been observed in Omdurman, in lower Egypt, and in Tunis.

In addition to being found in the spleen it has been demonstrated in the liver, kidneys, mesenteric glands, walls of intestinal ulcers, and in lesions of the skin including those of "Delhi boil" and scabies. The disease is very fatal. Quinine is nothing like so efficacious as a curative agent as in malaria. Some observers claim that the drug is a prophylactic. The mode of entrance of the parasite into the body has not been ascertained. It is thought probable that it enters by way of the skin. So far it has not been found in the urine or feces of infected individuals. The Indian physicians now do splenic puncture as a routine in all cases of splenomegaly and apparently meet with no untoward sequelæ. The cases usually show a leukopenia and the differential count reveals a marked reduction of the polymorphonuclears, and an enormous increase in the lymphocytes and particularly in the large mononuclears.

Various views have been advanced as to the nature of these bodies. Leishman thought that they were involution forms of the human trypanosome, but his view has been strongly opposed. In the hundreds of cases now on record no trypanosomes have been found in the circulating blood. Marchand and Leddingham supported Leishman's view. Laveran, who studied Donovan's specimens, thought that it was a form of piroplasma similar to the piroplasma bigeminum, the parasite of Texas cattle fever, and that they were sometimes contained in the red cells. Ross, supported by the majority of observers, thinks that we have to deal with an entirely new genus of the sporozoa.

The suggestion has been made that the splenomegalies of splenic anæmia and Banti's disease may be due to infections with this parasite. Additional interest is thus added to these diseases in this country.

**Removal of the Biurate Deposits and Excision of the Articular Capsule in Gouty Arthritis of the Big Toe Joints.**—RIEDEL (*La Semaine Médicale*, October 5, 1904), of Jena, reports two cases in which this operation was performed in gouty patients, with excellent results. He operated on his first case in 1882. The patient was a man, aged forty-five years, who was suffering from an attack of gouty arthritis of the right big toe joint. He remained perfectly well until 1896 without any recurrence of gouty attacks. In 1897 he had a vertebral arthritis and died of some unknown cause. The second case was a woman, aged seventy years, on whom he operated in 1894. This was her initial attack of gouty arthritis, which also affected the right big toe joint. There was never any return of the arthritis, the patient dying of aortic stenosis in 1902.

In both cases Riedel suspected that he was dealing with an acute suppurative bursitis in which the bursa communicated with the cavity of the big toe joint. He was surprised to find that it was actually a gouty arthritis with extensive deposits of biurates in the bursal sac and joint capsule. The bursa and entire joint capsule were excised in both cases, the ends of the bones not being removed. The edges of the incision were brought together but not sutured. Healing was perfectly satisfactory. The operation is recommended only for cases where the gouty attacks have been confined to the big toe joints. It is contra-indicated in a polyarthritis.

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**Studies on the Tuberculin Reaction.**—TRUDEAU, BALDWIN, and KING-HORN (*Journal of Medical Research*, August, 1904, vol. xii. p. 169) have carried out a series of experiments on guinea-pigs and rabbits, which are much less susceptible to tuberculin than human beings, with the object of better understanding the nature and specificity of tuberculin. Regarding the effect tuberculin has in spreading tuberculosis, they find that there is no such tendency in the case of corneal tuberculosis of the rabbit's eye, but that, on the contrary, as they had previously observed, there was a favorable absorptive influence on the diseased focus. Extirpation of a tuberculous focus was followed by loss of reaction—susceptibility to tuberculin. They conducted a series of experiments to ascertain whether specific tubercles are necessary for a positive reaction. Berkefeld filter capsules containing tubercle bacilli were introduced into the peritoneal cavity of rabbits. These capsules prevented the bacilli from coming into direct contact with the tissues, but by dialysis permitted the soluble products of the bacilli to pass through these walls. Some time after these had been introduced the animal was injected with tuberculin. It was found that the dialysable products failed to produce any local reaction about the capsules and the temperature elevations gave no certain evidence of susceptibility of these animals to tuberculin. The writers conclude that the presence of tubercle bacilli or substance in the tissues appears necessary to a true tuberculin reaction. The latter is apparently not due to the action of an enzyme. In support of this view is the fact that injections of trypsin failed to produce reactions when injected into animals with tuberculous abscesses. The tuberculin reaction may begin as early as the fourth or fifth day after infection with tubercle bacilli, but is constant after the thirteenth or fourteenth day. They were not able to conclusively demonstrate what constituent of the tubercle bacillus is responsible for the occurrence of the tuberculin reaction.

## THERAPEUTICS.

UNDER THE CHARGE OF

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ASSISTED BY

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**Results of Radiotherapy in Leukæmia.**—DR. FRIED has treated two cases of leukæmia by this means and has produced a considerable improvement in both. The patients were forty-six and fifty-nine years of age. Under the x-ray the white blood cells, which had been 62,000 in one case and 132,000 in the other, became normal or nearly so. The red cells and hæmoglobin were increased. The spleen diminished in size. The general condition improved, and in one case the weight was increased. These results were obtained in a short time and were such as no other treatment has been able to give. There were no unpleasant after-effects worthy of notice.—*Münchener medizinische Wochenschrift*, 1904, No. 40, p. 1772.

**The Serum Therapy of Typhoid Fever.**—PROF. CHANTEMESSE gives as the mortality in typhoid fever treated by his serum 4 per cent. The statistics are from 523 cases observed from April 1, 1901, to October 26, 1904. He has collected the statistics of 2618 cases treated at various hospitals in Paris, and finds the mortality to be 18 per cent. He replies to the statement made by some, that his good results are due rather to hydrotherapy than to the serum, by the assertion that where baths alone are used, the statistics show a mortality of 18 per cent. In 1902 he stated that serum therapy in connection with proper bath treatment should reduce the mortality from typhoid fever to 4 per cent. or 5 per cent., and, in the light of the results obtained since that time, he sees no reason to change his opinion. The serum employed is obtained from horses immunized by injections of a soluble typhoid toxin. Under the administration of the serum he considers that the liability to intestinal perforation is diminished from 2.6 per cent. to 1.6 per cent., and he has never observed perforation in a case injected before the seventh day of the disease. An interesting fact in connection with the serum treatment is that the agent should be given in smaller doses to the severe cases than to those of the ordinary type.—*La presse médicale*, 1904, No. 86, p. 681.

**Cryogenin and Typhoid Fever.**—DR. BOUTTEVILLE (*Thèse de Paris*, 1904) believes that the bath treatment is the method of choice, but if the baths are contraindicated or ineffective, we may have recourse to antipyretics. The author gives the results of a series of cases in which cryogenin was used. The drug was administered as follows: 15 grains on the first day, 9 grains on the second, 6 grains on the third, then from 3 to 6

grains daily, depending on the effect produced. Under this treatment the dryness of the tongue, the vomiting, and the nervous symptoms, nervousness, insomnia, stupor, and delirium disappeared. The cryogenin was given only in rebellious cases. In 14 out of 21 cases defervescence took place upon the twelfth day or earlier. In the others the fall of the temperature was more marked when a cold bath or a dose of quinine was preceded by the administration of cryogenin. The temperature would remain down for some hours. The author believes that one may use this drug in connection with bathing and hold the temperature in check better than when it is not given, that it will ameliorate the general condition and hasten defervescence, and that it is the drug of choice when baths are contraindicated. No bad effects were noticed due to its use, and it has a very certain effect in the fever of convalescence.—*Revue de thérapeutique*, 1904, No. 21, p. 735.

**Fresh Air in Nervous Cases.**—DR. VAN OORDT considers that treatment by means of rest in the open air, like that prescribed in tuberculosis, gives excellent results in the nervous complications of the infectious nervous disorders of digestion accompanied by emaciation; insomnia, cardiovascular neuroses, medullary irritability, and tabes are also indications. In hysteria, neurasthenia, neuralgia, migraine, and obsessions this treatment is without result.—*Zeitschrift für diätetische und physikalische Therapie*, 1904, No. 5, p. 281.

**Pulverized Antitetanic Serum in the Prophylaxis of Tetanus.**—M. LETULLE employs upon every suspicious wound a dressing prepared as follows: After thorough disinfection of the wound it is plentifully sprinkled with dry pulverized antitetanic serum and covered with a protective dressing of sterile cotton or gauze. The dressing is allowed to remain twenty-four hours, and if suppuration takes place it should be renewed as above until all pus has disappeared. The procedure has no disadvantages, it is not followed by erythema or arthralgia, and, in view of its simplicity and the results attained, the author believes that it should be employed as a routine on all wounds that have any possibility of having been infected with tetanus.—*La presse médicale*, 1904, No. 57, p. 452.

**Diphtheria Antitoxin in Ozæna.**—DR. TARNOWSKI has succeeded in arresting a beginning case of this affection by a single injection of 1500 units of antitoxin. In a second case, which had been treated by sodium sozo-iodolate for a considerable period without effect, 1500 units in eight days produced a permanent result. In a third case of forty years' standing no definite success was attained, but the production of crusts was lessened to a great extent. The author considers that this method of treatment is worthy of further trial.—*Deutsche medicinische Wochenschrift*, 1904, No. 23, p. 850.

**The Serum Therapy of Rheumatism.**—DR. SCHAEFER has observed the effects of Menzer's serum in six cases. None of these was subjected to any other form of treatment. In most of the cases the injection was followed by some pain and urticaria. These symptoms were, however, not of sufficiently unpleasant character to necessitate a cessation of the treatment. In four of the patients the disease was in the chronic

stage, and the serum wrought a cure within five days. No bad effects upon any of the bodily functions were noticed. In a boy, aged thirteen years, with a rheumatic mitral insufficiency, the cardiac symptoms were greatly relieved. The quantity of serum administered was from 15 to 75 minims every two days, depending upon the age of the patient and the reaction produced.—*Die Therapie der Gegenwart*, 1904, No. 3, p. 106.

**Sodium Biborate in Epilepsy.**—DR. F. HOPPE finds that in certain epileptics the bromides do not yield good results, and are not well borne, because of complications such as renal insufficiency, circulatory disturbances, or digestive disorders, especially hyperchlorhydria. In such cases he has used borax, and to twelve patients he has given from fifteen to forty-five grains a day. From his results he concludes that borax is unquestionably contraindicated where any insufficiency of the organs of elimination is present. In five of the patients very good effects were noticed. In one of these, a corpulent individual, suffering also from anæmia and hyperchlorhydria, the condition was materially improved, the seizures became more rare, and the body weight became less. On this patient alone did the drug act as a diuretic. The patients were given five grains three times a day with no unpleasant effect. Borax was also tried for six weeks in cases of uncomplicated epilepsy, but no amelioration was noted, and the bromide treatment was resumed. In conclusion, the author affirms that borax has no specific action in epilepsy, but may act well in cases complicated with gastric disorders, especially hyperacidity.—*Berliner klinische Wochenschrift*, 1904, No. 27, p. 730.

**Mercurial Injections in Syphilis.**—DR. LEREDDE advises in cases of syphilis which resist moderate doses of mercury and will tolerate the drug in large quantities, the use of the benzoate or the biniodide,  $\frac{1}{8}$  to  $\frac{1}{2}$  a grain hypodermically. This dosage, carefully increased, is unlikely to cause stomatitis and obviates the inaccuracy and inconvenience of inunctions. The author asserts that the use of injections should always be the treatment of choice in syphilis.—*Revue pratique des maladies cutanées*, 1904, No. 6, p. 186.

**Theocin-sodium Acetate.**—DR. J. MEINERTZ, after experimenting with this agent upon a series of patients, concludes that it is of considerable value in properly selected cases, especially in œdema and dropsy of cardiac origin. In order to get its best action there must be a considerable blood pressure, consequently in many cases its employment in combination with digitalis is advisable. This salt seems to be less likely to be attended by unpleasant after-effects than theocin.—*Therapeutische Monatshefte*, 1904, No. 6, p. 275.

**Rheumasan.**—DR. F. KOBISCH employs this agent, which is a 10 per cent. of salicylic acid ointment in superfatted soap, in various painful chronic conditions, such as polyarthritides, sciatica, lumbago, tabes dorsalis, gout, and neuritis, in the following manner: About 2 drachms are thoroughly rubbed into the affected part, which is then covered with a thin layer of cotton, which, after twelve hours, is removed. The skin is then washed, but not entirely dried, and a second inunction

is given. This procedure is repeated night and morning for two days, and after a two-day interval is renewed. In a few cases an irritation of the skin is produced. That the salicylic acid is absorbed is proven by the fact that it may be demonstrated in the urine about four hours after a treatment.—*Deutsche medicinische Wochenschrift*, 1904, No. 38, p. 683.

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**Internal Treatment of Pleurisy with Effusion.**—DR. LEWASCHEW states that it is not rare to observe an arrest of the disease following the observance of proper hygiene and the suppression of the causes predisposing to the inflammation. He regards the use of counter-irritant local applications as useless in most cases as far as favoring the absorption of the fluid is concerned. With regard to internal treatment he considers the salicylates to be most effective in limiting the inflammation and causing the absorption of the fluid. Sodium salicylate is the preparation of choice and if it does not produce the desired result in two or three weeks more active treatment is necessary, that is to say, thoracocentesis. The dosage of sodium salicylate recommended by the author is  $7\frac{1}{2}$  to 12 grains, four to six times a day, or less than this quantity in women or feeble patients.—*Wiener Medicinische Presse*, 1904, Nos. 37 and 38, pp. 1741 and 1797.

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**Hetol in Pulmonary Tuberculosis.**—DR. T. BARRETT HEGGS cites 7 cases which were treated by intravenous injections of hetol (synthetic sodium cinnamate). In all of them the tubercle bacillus was present in the sputum. Two of the cases were injected for about six months and the others for six or seven weeks. The blood for counting was taken four hours after a meal on alternate days in each case. The technique of the injection was simply to be certain that skin and instruments were surgically clean and to inject the drug into any sufficiently large vein of the arm. The method of graduated increase of dose on alternate days was followed and the maximum dose varied from 20 to 50 milligrams, never getting any ill effects. The leukocytosis was not in proportion to the amount of the injection. The maximum leukocytosis was generally obtained with about 20 milligrams. In all cases the injections were followed by definite leukocytosis. Often the normal count was doubled. In every case marked improvement followed the treatment, although some of the patients were taking creosote and cod-liver oil as well as the injections of hetol. The author's results lead him to the opinion that this remedy, though not a specific, is a useful adjunct to any other treatment of tuberculosis.—*Lancet*, 1904, No. 4234, p. 1136.

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**Mercurial Inunctions in Syphilis.**—DR. N. P. FETSCHENKO after experimenting upon 150 patients with different mercurial ointments with the idea of reporting upon their absorption, states less of the unguent is absorbed than one would suppose. Of blue ointment, for instance, about 25 per cent. is absorbed and that of a preparation not made up with lanolin. Freshly made ointments and those containing lanolin are very feebly absorbed. Resorbin and vasogen, especially the former, are excellent vehicles. It is useless to prolong the rubbing more than one-half an hour or to increase the quantity of the ointment beyond a certain point. The skin will absorb just so much and no more. The



skins of those who wash frequently have the best absorptive powers, and absorption is at its maximum after a hot soap and water bath. In summer absorption is more active than in winter and energetic friction as well as the addition of gaultheria or menthol added to the ointment aids absorption.—*Wiener Klinisch-therapeutische Wochenschrift*, 1904, No. 15, p. 419.

#### Physical Methods in Treatment of Chronic Articular Rheumatism.—

DR. N. DOHAN considers that too little attention is paid to physical methods in the management of this affection. He recommends that the diseased joint be subjected to an induced current for eight to ten minutes. This relieves the pain to a considerable extent. Then the joint is bathed in water at 58° to 60°, or swathed in bandages wet with cold water. After the pain has been benefited by these procedures an electric light bath, lasting from eight to ten minutes is prescribed, followed by a cold douche to the joint. After this the joint should not be dried immediately. During the treatment a more or less rigid milk diet is advised.—*Blätter für klinische Hydrotherapie*, 1904, No. 9, p. 197.

**Antistreptococcus Serum in Puerperal Sepsis.**—DRS. H. PILCER and M. EBERSON conclude a study of the effect of this agent upon 28 cases with the following statements: 1. That Marmorek's antistreptococcus serum is not a specific against all forms of puerperal sepsis, but it is a powerful adjunct to other treatment of this infection. 2. The serum acts by stimulating the formation of leukocytes in the diseased organism, and for this reason it is indispensable in puerperal fever. 3. The serum produces a feeling of well-being in the patient which is a point in favor of its administration in connection with other therapeutic agents. 4. To produce the best effects the serum must be injected in sufficiently large quantity, the average dose being from 1½ to 3 ounces.—*Therapeutische Monatshefte*, 1904, No. 10, p. 509.

**Age Limits in Cold Water Therapy.**—DR. WINTERNITZ protests against the prejudice which exists against the employment of cold water in anæmic and debilitated persons on the ground that it extracts body heat. On the contrary, according to him, the cold water augments the production of heat. In infants cyanotic and cold from gastro-enteritis he has obtained remarkable results by means of friction with cloths wrung out in cold water. Such applications provoke a considerable excitation of the organic functions and are indicated in the infant in all torpid conditions and circulatory disturbances. He considers extreme youth no contraindication to the application of cold water. Likewise in old age he recommends rapid local use of cold water. Arteriosclerosis is no contraindication. At first sight this would not seem true for cold increases the blood pressure, already below normal in atheromatous patients. The author recognizes two varieties of arteriosclerosis, one with increased blood pressure, the other, and these are the more gravely affected, with an arterial pressure below the normal. But quick applications of cold lower the pressure in the first group and elevate it in the second; in the former class the hydrotherapy stimulates inhibition, in the second it excites the organism.—*Blätter für klinische Hydrotherapie*, 1904, No. 8, p. 173.

## PEDIATRICS.

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UNDER THE CHARGE OF

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**Heart Complications in Diphtheria. A Clinical Study of 946 Cases.**—FRANKLIN W. WHITE and HOWARD H. SMITH (*Boston Medical and Surgical Journal*, 1904, vol. cli., No. 16) give their clinical observations of nearly 1000 cases of diphtheria treated at the Boston City Hospital during one year. The cases were studied principally to determine the character and frequency of heart lesions and their practical importance in prognosis and treatment.

About 5 per cent. were less than one year of age, 40 per cent. less than five years, and about 70 per cent. less than ten years old. In one-quarter of the cases the illness was severe; more than one-half of these, or 132, proved fatal. Only a fourth of the deaths were from heart complications; the most frequent cause was bronchopneumonia following intubation or tracheotomy. These facts are opposed to Villy's statement that the majority of fatal cases of diphtheria die on account of heart complications.

The patients came mainly from the poorer classes, where treatment is likely to be deferred, so that most of them did not receive antitoxin until the second or third day; and of the severe and fatal cases, at least two-thirds were four, five, or more days without antitoxin treatment.

The symptoms and physical signs of cardiac disturbance are treated at length. About 60 per cent. of the cases showed irregularity of the pulse. This sign was more frequent in the younger patients, and was observed in the severe, moderate, and even mild cases. It was very variable in its appearance and duration. The rhythm would change from marked irregularity to perfect regularity often within half an hour.

The number of patients with heart murmurs is a striking feature of the study: 878 had heart murmurs at either the apex or base, or 94 per cent. of the cases where the condition of the heart was carefully observed and recorded. These murmurs were not faint or doubtful, but for the most part were loud and blowing, and in each case were confirmed by two or three competent observers. The murmurs were all systolic in time, with the exception of those in a few cases of chronic heart disease. They were usually heard at the apex, frequently transmitted to the axilla, and associated with accentuation of the pulmonic second. The majority were accompanied by irregular heart action and outlasted the fever. In 90 per cent. of the patients with murmurs, this sign was present upon entrance to the hospital, and in about 78 per cent. of the cases one or more murmurs were present at discharge. The duration

of the murmurs after leaving the hospital is unknown, except in a few instances. Five or six of the patients were examined some eight months after their discharge, and each showed a murmur; two of these, in addition, having cardiac enlargement and evidences of myocarditis.

As to prognosis, the author believes that the mere presence of a murmur has little of value, as the sign is so nearly universal.

The clinical course of the cases does not explain the cause of these murmurs. Pathological studies show that they are probably due largely to relative mitral insufficiency resulting from changes in the heart muscles, or to changes in the innervation of the heart. Autopsies have shown that endocarditis and pericarditis are extremely rare complications of diphtheria. Cardiac enlargement was infrequent, and was found only in the severe cases. The writers believe that the frequency of acute dilatation and syncope has been exaggerated, as almost all of their fatal cases showed a gradual heart-failure. They agree with Poynton that dilatation of the heart is not so marked in diphtheria as in rheumatic fever.

In the patients with chronic heart disease, 17 in number, the course of the illness was no more severe than in the average patient.

The cases with heart complications are divided into three separate types. The first and most serious type have gallop rhythm, vomiting, epigastric pain and tenderness, run a short course of two or three weeks, and die in the majority of cases. The second type lasts for weeks or months, with a rapid, regular, or irregular heart, easily affected by slight exertion, and gradually becoming normal in rate. There are few other important symptoms. The third type is rare; its main feature is a very slow pulse, occurring at the end of the second or the beginning of the third week. There is a marked decrease in rate over a period of three days, the pulse dropping from 110 or thereabouts to 30 or even 20. The subjective symptoms are slight until the pulse reaches a low level (40), when signs of prostration set in. The sounds are weak, and a moderate degree of dilatation occurs. There were 3 such cases in the series, all fatal; 36 of the cases were considered as having serious heart complications. Two-thirds of these patients died. Four-fifths of the fatal cases had no treatment until after the fourth day.

The most important cardiac symptom is gallop rhythm; this was found in all the 36 cases. The murmurs usually become indistinguishable upon the appearance of this symptom.

Late vomiting is the next important symptom. It was present in all but 4 of the fatal cases. In nearly every case the appearance of the gallop rhythm preceded the onset of vomiting from one to four days.

The next symptom is epigastric pain and tenderness. Nine-tenths of the patients who had this symptom died. This symptom usually was closely associated in time with the appearance of vomiting, either a day or two before or a day or two after.

Palatal paralysis was noted in 19 of the severe cases and in 10 of the fatal cases.

The importance of these symptoms (gallop rhythm, late vomiting, epigastric pain and tenderness) as danger signals and their value in prognosis are shown by the fact that they were very frequent in the severe and fatal cases, and very rare in those that recovered.

As to the treatment, rest in bed is considered of most importance in dealing with heart complications. The figures show that the serious

complications nearly always develop within three weeks from the onset of the illness. Mild cases are allowed to be out of bed at the end of two weeks. The presence of murmurs and a slight degree of irregularity are no contraindication if the first sound is strong and the heart is not dilated.

The severe cases must be watched for four or five weeks, but after this time the danger from serious heart complication is usually over. In cases with gallop rhythm, absolute rest in bed, upon a liquid diet, is necessary. At the first appearance of vomiting food should be given by rectum. Strychnine gives the best results. Alcohol and digitalis are not well borne. Morphine may be necessary. The after-treatment of all except the mild cases consists in watching the effect of mild exercise, upon the heart for several months, and grading it to meet individual requirements.

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## OBSTETRICS.

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UNDER THE CHARGE OF

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**Spontaneous Rupture of the Uterus after Cæsarean Section.**—KERR (*British Medical Journal*, June 18, 1904) reports the case of a patient upon whom he had previously performed Cæsarean section, employing the transverse incision across the fundus. The patient was not sterilized. She was admitted to the hospital in a succeeding pregnancy, estimated at the thirtieth week. She was given an enema, after which she complained of pain in the abdomen, but shortly afterward fell asleep. The next morning the pain extended over the entire abdomen, tenderness gradually developed, the pulse rose to 90, the temperature became subnormal, and the breathing more rapid. The patient lay with her feet slightly drawn up, and the fetal parts could be felt with great distinctness through the abdominal wall. There was some blood-stained vaginal discharge.

On performing abdominal section a large quantity of dark-colored blood escaped, and the foetus and placenta lay in the abdomen with the membranes unbroken. The uterus was retracted behind the foetus, and had a transverse rupture through the scar of the previous operation. Hysterectomy was performed, leaving a stump of cervix, and the patient made a good recovery.

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**Cæsarean Section for Contracted Pelvis.**—At a recent meeting of the Obstetrical Society of London (*British Medical Journal*, October 22, 1904), KERR based his paper upon 30 cases of Cæsarean section. His maternal mortality was 6.6 per cent. His morbidity based upon a temperature of 100.5° on more than one occasion was 26 per cent.

Of the two cases fatal, one died on the fifth day from septic peritonitis, the other the day after the operation from the parting of several uterine stitches with free bleeding. He believed that if a patient came under the care of the physician sufficiently long to receive thorough preparation, celiohysterotomy should be done. Where, however, time for preparation is scanty and the condition of the uterus uncertain, celiohysterectomy is the operation of choice.

Hermann believed that early operation was very safe and late operation dangerous. Griffith had lost a case in Cæsarean section and did not think vaginal douches proper unless there was distinct evidence of infection. Where sterilization was desired he ligated the tubes with fine silk. Routh would allow the patient to choose the method of operation and if sterilization was admissible, he would accomplish it by removing the uterus, leaving the ovaries. Spencer had performed eight operations without mortality.

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**The Bladder and its Disorders During the Puerperal Period.**—In the *Monatsschrift für Geburtshilfe und Gynäkologie*, 1904, Band xx., RUGE contributes an interesting paper upon this subject.

Writers have formerly ascribed most disturbances in the bladder after labor to overdistention. Some have given abdominal pressure undue importance. His researches led him to believe that the mechanism of labor is such in all cases where the child is delivered through the vagina, that strong pressure is brought to bear upon the bladder at the neck and trigonum, and that this pressure causes lesions which produce characteristic results. The longer the labor, the greater the pressure. The proportionate size of the head and pelvis, the length of time that the head is in the pelvis and especially the length of time that the head remains upon the pelvic floor are important factors. The longer the expulsive stage of labor, the greater the danger of injury to the bladder.

The anatomy of the bladder is such as to produce the characteristic lesion described as bullous œdema. In other cases œdema of the bladder wall is frequently found. Areas of darkened color with swelling of the mucous membrane are observed by the cystoscope and persist from four to six weeks after the birth of the child.

Hemorrhage may also occur from the sphincter of the bladder to the posterior wall. Such hemorrhage is beneath the epithelium, its areas of various shapes. The color changes during the process of recovery.

When his cases are reviewed, it is found that lesions of the bladder are not confined to those cases of labor terminated by difficult obstetric operations. Pelvic contraction was not present in these cases. Where injuries were but slight, no symptoms were present; where they were severe, the patient had retention of urine or painful micturition. Changes in the urine were present, dependent upon the altered condition of the mucous membrane of the bladder. The bladder was especially liable to infection and hence the utmost precaution in the use of the catheter was imperative. Lesions of the ureters and urethra, similar to those found in the bladder, were also observed.

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**Lithopædion Forty-one Years in the Abdominal Cavity.**—In the *Journal of Obstetrics of the British Empire*, October, 1904, HAULTAIN reports the case of a patient dying of cardiac disease who had within the abdomen a lithopædion forty-one years.

On post-mortem examination, the calcified foetus was found behind the uterus, densely adherent to the intestines and surroundings. The head was downward and there was no enveloping sac. The uterus was atrophied and adherent to the front of the foetus. The patient was well aware of the presence of the child and had frequently remarked upon it. She had occasional attacks of abdominal inflammation, but was usually in good health.

The foetus was in the usual attitude, the limbs were in absolute preservation, the nails projected over the finger-tips. On the back, scalp, and breech the tissue seemed to be of normal thickness.

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**The Albuminuria of Pregnancy.**—In the *American Journal of Obstetrics*, September, 1904, LITTLE gives the results of the examination of urine in pregnant patients in the obstetric wards of the Johns Hopkins Hospital. Although the records of 960 cases were available, they were not considered sufficiently exact for purposes of investigation. The urine was examined in 100 consecutive cases in the most minute and painstaking manner and the results are stated.

In catheterized specimens of urine from about one-half of all pregnant women, equally in primiparæ and multiparæ, albumin is found. In urine which is voided, albumin is more frequent in the cases of multiparæ. Casts are more often found in the urine of multiparæ. Labor produces a decided increase in albumin alone and casts and albumin especially in primiparæ. The increased blood pressure and muscular contraction of labor account for this. Casts without albumin are often found during pregnancy, labor, and the puerperal state. In the puerperal state, albumin and casts occur less frequently than in pregnancy. In no case was albumin present during pregnancy and absent at the time of labor, while casts during pregnancy and absent at the time of labor were found in only three cases. Two-thirds of the cases which showed casts at the time of labor had albuminuria during pregnancy.

As regards the pathological conditions attended by the presence of albumin it was found in 25 cases of eclampsia and 9 cases of threatened eclampsia. When eclampsia occurred, casts were present in 22 out of 23 cases. Pernicious nausea showed much albumin and many casts. During the puerperal period, albumin and casts persisted longest in those cases in which they had been found during pregnancy. Albuminuria was present in 4 cases of abortion, 2 from syphilis, 1 from typhoid fever, and 1 from chronic nephritis. Albuminuria without complications did not in any case produce abortion. Nausea and vomiting was present in 20 per cent. of primiparæ and 33½ per cent. of multiparæ who at some time had albuminuria. Œdema was present in one-third of these cases.

So far as the association of albuminuria with renal disease is concerned, it is pointed out that the albuminuria of pregnancy is the result of a toxæmia and not of a true nephritis. The kidney of pregnancy is the result of a degenerative process, resulting from the circulation of blood laden with toxins through the kidney.

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**Spontaneous Rupture of the Pregnant Uterus through the Scar of a Former Cæsarean Section by Transverse Incision.**—In the *Zentralblatt für Gynäkologie*, 1904, No. 44, EKSTEIN reports what he describes as the first spontaneous rupture of the scar occurring after this operation.

Regarding the condition of the scar after Cæsarean section, there are various observations: Brünings, in a repeated Cæsarean section, found the scar of the first operation greatly thinned. Gueniot, seventeen months after a Cæsarean section, found stitches still remaining in the scar. Two years after Cæsarean section Everke found no stitches in the scar. Czyzewicz, four years after a Cæsarean section, in performing a second, found the scar white and glistening and the anterior uterine wall greatly thinned. Three and a half years after Cæsarean section Rühle found the scar of the former operation so thin that he performed hysterectomy. Lihotzsky, seven years after Cæsarean section, found that silk sutures had been completely absorbed. Brown and Saenger believe that in sixty days after operation the greater part of silk stitches are absorbed. Schneider found, two years after Cæsarean section, no trace of the former scar. Staudc, two years after operation, found the scar of the first a narrow white line and no silk sutures remaining. Löhlein performed 3 successful Cæsarean operations upon the same patient. He observed no tendency to dilatation of the scar. These operations were performed by the longitudinal incision.

Regarding the scar in the transverse incision, Ludwig found silk sutures in the scar one and a half years after operation. Flateau, two years after operation, could find no trace of sutures in the transverse incision. It is evident from these reports that the scar after operation differs greatly in different cases. Spontaneous rupture through the scar is, however, of rare occurrence. Woyer reports a case of spontaneous rupture in a uterus pregnant, with twins, in a patient on whom Cæsarean section had been performed three years previously. The uterus had been closed by thirty silk sutures. Guillame observed rupture through the scar of a former Cæsarean section three years after operation, occurring at the seventh month of pregnancy. Targett reports a case of rupture through a Cæsarean scar. Everke exhibited a uterus with spontaneous rupture through a Cæsarean scar, the operation having been performed four years previously by the Sacnger method. In this case the entire scar separated and the placenta was found in the point of rupture. Meyer reports 2 cases; in the first, rupture of the abdominal and uterine wound on the ninth day after operation, the patient recovering; in a second operation on the same patient two years later there was no trace of the scar of the first operation. A longitudinal incision was again made, closed with eight silk sutures, with good result. In a second case, Cæsarean section had been done for contracted pelvis and the uterus closed with catgut suture. Two and a half years afterward a second operation was done, and rupture in the old scar was found with some protrusion of placenta.

There is reason to believe that the attachment of the placenta over the scar favors the occurrence of rupture. Some have thought that the anterior incision is less likely to rupture, because adhesions frequently occur between the uterus and abdominal wall, thus strengthening the uterine wall at this point.

Ekstein's case is as follows: The patient, aged thirty-three years, was in her fourth pregnancy. The first and second pregnancies were terminated by craniotomy. The third ended by Cæsarean section, and the patient was advised for subsequent pregnancy to return to the hospital for the induction of labor. At nine months' gestation after exertion the patient was brought to the hospital, stating that she had felt no

movements of the child for two days. On examination the patient was evidently in the ninth month of gestation; the abdomen was greatly distended, so that a thorough examination was impossible. Neither heart sounds nor uterine souffle could be heard. The abdomen was very sensitive on pressure. The heart and lungs of the mother were practically normal, although the pulse and respiratory rate were increased. The tongue was heavily coated, and there was frequent vomiting of a greenish-yellow mucus. The patient's temperature was practically normal. The vomiting and abdominal distention increased, and the pulse rose to 140. Upon operation decomposed blood was found in the abdomen, the child had entirely escaped with its appendages through the uterus, the placenta lay upon the right side, the child with its back toward the left and posteriorly, the head near the left iliac bone. The uterus had firmly contracted and the scar of the former Cæsarean section had completely ruptured and a portion of the membranes remained within the rupture. The child was dead, the amniotic liquid a brownish-gray and discolored. The child and blood were removed from the abdomen and hysterectomy performed. The patient died shortly after the operation. Examination of the uterus showed that suture material had entirely disappeared from the scar. The placenta had been attached upon the anterior wall of the uterus and partially over the scar. Microscopic examination showed that the decidua extended over the entire laceration and upon the anterior wall. The uterus was remarkably firmly contracted.

The Cæsarean operation performed in the preceding pregnancy had been by the transverse incision at the fundus, silk had been used as suture material in the muscle, and catgut had been employed for peritoneal surfaces. This operation was performed about three years before the rupture of the uterus.

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## GYNECOLOGY.

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UNDER THE CHARGE OF

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OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

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**Lipoma of the Abdomen.**—MICHEL (*Zentralblatt für Gynäkologie*, 1904, No. 41) reviews the literature of the subject thoroughly. He includes subcutaneous, intramuscular, pre- and retroperitoneal lipomata. The latter are of especial interest from a diagnostic standpoint, and are quite rare. The retroperitoneal variety is usually unilateral, developing either from the perirenal fat or between the peritoneal and abdominal wall in the iliac fossa, in the broad ligaments, or between the rectum and bladder. They may be sessile or pedunculated, single or multiple, and may reach an enormous size (twenty to sixty pounds). They are often so soft as to give the impression of fluctuation, hence



they have frequently been mistaken for ovarian cysts. They differ from the latter neoplasms in being less elastic and independent of the uterus, while the intestines lie in front of them or at one side, as in the case of renal growths. Peritoneal tuberculosis, cysts of the mesentery, and even the pregnant uterus may be confounded with lipomata.

The principal symptoms are those due to pressure on the hollow viscera and bloodvessels. The prognosis after operation for the removal of retroperitoneal lipomata is grave, only 4 recoveries having been reported out of 11 cases.

The pre-peritoneal variety develop between the peritoneum and transversalis fascia and grow into the abdominal cavity where they may become detached, so that it is difficult to distinguish them from hernia or fatty degeneration of the omentum. Through traction they may give rise to severe gastric symptoms. The writer reports an interesting case in which the diagnosis of ovarian cystoma was made. Various theories have been advanced regarding their origin, such as local disturbances of the circulation in the bloodvessels and lymph-vessels, reflex nervous conditions, or aberrant cells (*Recklinghausen*). Local irritation, heredity and struma have also been stated to be etiological factors. A direct relation between thyroid hypertrophy and lipomata has been claimed by several observers. The writer inclines to Ribbert's theory of fetal inclusion. The only treatment is surgical, especially in view of the fact that sarcomatous degeneration has been noted in some instances.

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**Adnexal Disease Due to Typhoid Fever.**—DIRMOSER (*Zentralblatt für Gynäkologie*, No. 40, 1904) reports a case of tubo-ovarian abscess in a virgin who had typhoid six months before. The characteristic bacilli were found in the pus. A similar case was reported by Koch, who inferred that the infection came through the intestine. The writer believes that the bacilli make their way through the lymph channels in the gut to the surrounding connective tissue and thus reach the ovary and tube, though the possibility of hæmatogenous infection cannot be denied.

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**Patent Urachus.**—SWIRT (*Nederl. Tijdschrift v. Geneesk.*; *Zentralblatt für Gyn.*, 1904, No. 41) reports the following cases:

1. The patient, aged fifty-eight years, entered the hospital on account of retention of urine, while urine dribbled from the umbilicus. An artificial vesicovaginal fistula was established, when the urachus closed spontaneously, and later the fistula also.

2. A girl, aged seventeen years, had constant dribbling of urine from the navel, blood escaping from the same opening at every menstrual period. The edges of the fistula were split and a purse-string suture was inserted, followed by primary union.

3. A boy, aged one and one-half years, had eczema of the navel with a discharge of offensive urine; he had also a marked phimosis. Circumcision failed to cure the fistula. As there was diastasis of the recti muscles, the umbilicus was excised and the opening of the urachus was successfully closed with a purse-string suture.

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**Treatment after Curettement.**—ORIA (*Rev. de med. y cir, Madrid*; *Zentralblatt für Gyn.*, 1904, No. 41) believes that sufficient care is not

given to the after-treatment of the patient. She should be kept in bed for three weeks after the operation. In proof of this he reports 400 cases from Madrazo's clinic, in not one of which were there any complications, nor was a second curettement required.

**Gynecology in Turkey.**—R. RIEDER-PASCHA in a report of the Gülhane at Constantinople calls attention to the fact that gonorrhœa is less common in Mohammedan women than in those of other sects. In the treatment of gonorrhœal endometritis the best results were obtained by applications of nitrate of silver, argonin, and formalin.

Cases of cancer of the cervix were rarely seen in an operable stage.

Retrodisplacements of the uterus were often an accompaniment of gastroenteroptosis and movable kidney, which the writer attributes to the vegetarian diet and chronic constipation so common in Turkish women, and to the fact that they are allowed to leave their beds too soon after parturition.

Pessaries are regarded with aversion by both native physicians and patients. Fibroids were comparatively rare except in negroes (4.9 per cent. of 952 patients), and were only operated upon when there was profuse hemorrhage or rapid growth. Total extirpation was usually performed with a mortality of 14 per cent. (!)

Conservative treatment of adnexal disease was the rule, only three abdominal operations being performed.

The report states that "parametritis" is the most common pelvic affection in Constantinople, local massage being a favorite method of treatment. All the cases of mammary cancer were received in an advanced stage.

**Ultimate Results of Abdominal Hysterectomy for Cancer of the Uterus.**—FREUND (*Zentralblatt für Gynäkologie*, 1904, No. 42) presented at a recent meeting of the German Medical Congress a patient whose uterus he had removed for cancer of the cervix and corpus uteri by the abdominal route, being the first successful case of total abdominal extirpation. The writer stated that he had from the beginning favored this method, though the subsequent bad results had rendered vaginal hysterectomy more popular. The fact that the pendulum had swung backward was a proof that the ultimate results of the vaginal operation had not been satisfactory. The importance of removal of the lymph nodes had been fully demonstrated, but this had only emphasized the fact that Freund's original operation was the correct method.

The reporter thought that surgeons should not be discouraged by the fact that the primary mortality of abdominal hysterectomy was still rather high. More favorable results could be expected provided that proper care was exercised in the selection of incipient cases.

Döderlein (*Ibid.*) reported 73 cases of hysterectomy from October, 1897, to January, 1900, with 15.8 per cent. cured; 10 patients who had cancer of the body of the uterus were entirely free from disease. Since January, 1902, the reporter had performed only the abdominal operation (112 cases), 30 per cent. of the patients being free from recurrence. In 26 out of 65 cases of cancer of the portio vaginalis (24.3 per cent.) cancerous lymph nodes were removed; in 29 per cent. of the cases of cervical cancer, and in 9 per cent. of those of malignant disease of the body of the uterus.

The fact that infected nodes were present in only 2 out of 23 cases of corporeal cancer showed that the latter could be treated equally well by vaginal hysterectomy.

Mackenrodt (*Ibid.*) stated that he had obtained 44 per cent. of permanent cures up to 1901 by vaginal igniextirpation. Since then he had operated in 71 cases, with a primary mortality of 19.7 per cent.; 77.4 per cent. were free from recurrence at intervals of one to three years, and 70.8 per cent. of all his surviving patients were well. In the discussion which followed Veit called attention to the high primary mortality (15 per cent.), which was due not so much to defective technique as to the disease itself; it will doubtless be lowered by better antiseptic preparatory treatment.

Wertheim stated that his percentage of cures after four years was 18.2 per cent. His primary mortality was 17 per cent.

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**Double Mammary Cancer.**—BECK (Inaugural Dis.; Abstract in *Zentralblatt für Gynäkologie*, 1904, No. 42) analyzes 61 cases, and concludes that cancer in the opposite breast is really a metastasis and not primary disease. Whether the lymph vessels connecting the mammæ serve as channels of infection or not has not been clearly demonstrated. The writer inclines to the view that cancerous emboli are carried from the original site of disease to the other breast, rather than to the theory of direct extension along the lymphatics.

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**Torsion of the Pedicle of Ovarian Cysts.**—TRANGENHEIM (Inaugural Dis.; *Zentralblatt für Gynäkologie*, 1904, No. 42) in reviewing the statistics of Olshausen's clinic found that in 971 ovariectomies torsion of the pedicle was found in 8.2 per cent., while in 101 cases of parovarian cyst 7 per cent. had twisted pedicles. Only 3 fatal cases were recorded: one from intestinal obstruction and two from peritonitis. The latter were in a hopeless condition before operation, as 17 other similar, but less severe, cases were operated upon successfully.

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**Laparotomy for Ruptured Ectopic Pregnancy.**—SEIDEL (Inaugural Dis.; Abstract in *Zentralblatt für Gynäkologie*, 1904, No. 42) analyzes 90 cases from the Berlin clinic, 52 of intraperitoneal rupture, 13 of tubal abortion and 15 undetermined. In 30 there was no vaginal hemorrhage whatever, and in only 2 was decidual membrane discharged. Menstruation was absent in 53 cases, delayed in 16, regular in 16, and scanty in 5. Laparotomy was the operation elected. The mortality was 14.4 per cent., 6.6 per cent. succumbing from the operation; 5.2 per cent. of the patients had a second extrauterine and 24 per cent. a subsequent normal pregnancy.

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**Perforation of the Uterus versus Sounding of the Tubes.**—THOM (*Zentralblatt für Gynäkologie*, 1904, No. 36) believes that most of the cases reported under the head of introduction of a sound into a dilated tube were really those of puncture of the uterine wall. He finds that experiments on the cadaver and living subject alike prove that it is impossible to introduce a sound into a normal tube from the uterine cavity. Only 2 previously reported cases (Bischoff's and Floeckinger's) are authentic, and in each of these there was a fibroid uterus, as well as dilatation of the distal ends. He reports 2 others, which prove that only

under abnormal conditions is sounding of the tube possible. In order to accomplish this, not only must the ostium uterinum, as well as the cornu, be dilated, but the wall of the tube must be capable of sufficient resistance, and the uterine cavity must be enlarged and the organ laterally displaced by fibroids or interstitial pregnancy.

**Adenomyoma of the Uterus.**—MEYER (*Zentralblatt für Gynäkologie*, 1904, N. 37) reports a case in which he found two small nodules from the posterior wall of the uterus, which microscopically consisted of fibromuscular tissue containing numerous groups of glands. The neoplasm had no relation to the endometrium. As they were diffuse and could not be enucleated, the uterus was extirpated.

The writer inclines to Recklinghausen's theory that they developed from the primordial kidneys, though it was possible that they had their origin in the endometrium (before or after birth), in the proliferated serous epithelium, or in the epithelium of Gärtner's ducts.

**Saenger Operations for Prolapsus.**—SCHEIB (*Monatsschrift für Geb. u. Gyn.*, Band. xviii, Heft 5) reports 141 cases, in 16 of which vaginofixation or ventrofixation was performed. In 65 patients who were kept under observation, 60 per cent. were cured.

**Disinfection of the Hands.**—SCHAEFFER (*Monatsschrift für Geb. u. Gyn.*, Band xviii, Heft 5), from experiments with sublamin, found that a 1 per cent. solution possesses a stronger bactericidal action than a 10 per cent. He regards alcohol as the best disinfectant of all, and prefers to simply wash his hands with hot water and alcohol.

**Adhesions of the Spleen and Uterus.**—IVANYI (*Szülés zet és Nögy.; Zentralblatt für Gynäkologie*, 1904, No. 37) reports the case of a patient, aged thirty-eight years, who had formerly suffered from malaria. She had a retroflexed uterus; attached to the left side of the fundus was a large, smooth tumor, the shape of the spleen. The diagnosis of dermoid cyst was made, and possibly wandering spleen. The latter was confirmed under anæsthesia. On opening the abdomen the enlarged spleen was found to be firmly adherent to the fundus uteri and omentum, with torsion of its pedicle. The adhesions were separated and ventrofixation was performed, the spleen being subsequently supported by a bandage.

**Ovarian Cysts of Unusual Size.**—SKUTSCH (*Zentralblatt für Gynäkologie*, 1904, No. 37) reports 2 cases of large ovarian cystomata, one weighing 83 and the other 100 pounds, both of which were successfully removed, the patients remaining in good health afterward. He adds that such large tumors are now rare, as they are usually recognized and removed early. It is only in women living in remote places in the country that they would be likely to grow so large.

**False Ova in Cancer of the Ovary.**—LIEPMANN (*Zeitschrift für Geb. u. Gyn.*, Band lii, Heft 2) calls attention to the fact that the appearances described by authors as persistent ova in cancerous ovaries are really products of degeneration, being cavities which contain bodies resembling primordial ova situated between the epithelial groups and processes.

## OPHTHALMOLOGY.

UNDER THE CHARGE OF

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**A Case of Choroidal Inflammation Caused by Excessive Use of the Eyes.**—ST. JOHN ROOSA (*New York Medical Record*, February 20, 1904) reports the case of a physician, aged forty-six years, who, after ten hours of almost continuous reading of rather but not excessively small type, discovered the following morning a very disturbing blur confined to the right eye. He took a trip on the water and was exposed to the glare, taking no particular pains to prevent its influence on his eyes. The blur continuing, the patient consulted Dr. Roosa six weeks later (October, 1896). Vision: right,  $\frac{20}{30}$ ; left,  $\frac{20}{20}$ . The vitreous of the right eye was so hazy that no good view could be obtained back of the fundus. He was not examined again until January, 1898, when the vision was found to be the same, the subjective blur persisting without change. The vitreous had quite cleared up, and there were several spots of choroidal atrophy. He was seen again December, 1903. The vision of the right eye was the same, and the same extensive choroidal changes (atrophy) were noted. The vision of the left eye was  $\frac{20}{15}$ .

The reporter remarks that although continuous use of the eyes on small objects is a recognized cause of inflammation of the eyeball, such results are rarely seen, the asthenopia accompanying excessive use usually causing the patient to desist before the danger-line has been crossed. It is also remarkable that the choroiditis came to an immediate standstill. It is interesting to note that the retina was unaffected, to any considerable degree, at least. It is also interesting to note that this was a traumatism rather than an infection, the former of which, with our present views upon infectious diseases, we are apt to ignore.

**The Innervation of the Pupil.**—PARSONS (*Roy. Lond. Ophth. Hosp. Rep.*, June, 1904) gives an exhaustive review and bibliography of a vast amount of research upon this subject, together with original experiments of his own. He sums up the results as follows: The iris contains a sphincter and dilator muscle, each of unstriated fibres. The sphincter is a compact ring of muscle near the pupillary margin. The dilator is a thin layer of muscle situated near the posterior surface, the constituent fibres being arranged radially. Each muscle has a separate and independent motor-nerve supply. Histological evidence alone has not succeeded in demonstrating beyond cavil the existence of a dilator muscle in the iris, but taken in conjunction with the physiological evidence it must now be considered proved. The histological difficulties are to be found in (1) the proof of the pres-

ence of radial muscle fibres other than those in the walls of the vessels, and in (2) the interpretation of the nature of the cells forming the posterior layers of the iris. These cells—*i. e.*, the anterior layer of retinal pigment epithelium—act as a dilator muscle. On bleaching and staining they resemble in all respects unstriated muscular fibres. Evidence also exists to show that the sphincter pupillæ is likewise derived from the retinal epiblast. These muscles would therefore resemble the arrectores pilorum of the skin in being formed from epiblast. The physiological evidence in favor of a distinct dilator is stronger than the histological, being indeed quite conclusive. The sphincter is innervated by the third cranial nerve, the pupil constrictor fibres originating in the third nucleus in the floor of the aqueduct of Sylvius, passing out of the mesencephalon in the third nerve as far as the orbit. The fibres here pass into the branch which supplies the inferior oblique, leaving it by the short root of the ciliary ganglion. From the ciliary ganglion they pass by the short ciliary nerves to the eye, piercing the sclera around the optic nerve, and thence forward in the choroid and ciliary body to the iris.

The dilator pupillæ are supplied by the cervical sympathetic nerve. The dilator tract probably commences in the neighborhood of the third nucleus in the mesencephalon, passing through the medulla oblongata, where its exact path is still unknown, into the lateral columns of the cord. The fibres leave the cord by the ventral routes of the first three thoracic nerves (cat, dog, ape), enter the rami communicantes, and run to the first thoracic or stellate ganglion. From here they mostly pass into the anterior limb of the annulus of Vieussens, though some run in the posterior limb. They pass up the neck in the cervical sympathetic to the superior cervical ganglion. From here the dilator tract enters the skull by the cervico-Gasserian strand, running independently of the carotid plexus. It joins the Gasserian ganglion and passes thence into the first or ophthalmic division of the fifth nerve, following the nasal branch, which it leaves finally to enter the long ciliary nerves, thus avoiding the ciliary ganglion. The long ciliary nerves enter the eye on each side of the optic nerve, and, running forward between the choroid and sclerotic, pass through the ciliary body to be distributed to the iris.

Constriction and dilatation of the iris are brought about respectively by three factors which are effectual in diminishing degree in the following order: Constriction—(1) contraction of the sphincter muscle; (2) relaxation of the dilator muscle; (3) dilatation of the bloodvessels. Dilatation—(1) contraction of the dilator muscle; (2) relaxation of the sphincter; (3) constriction of the bloodvessels.

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**Opaque Nerve Fibres.**—HAWTHORNE (*The Ophthalmoscope*, September, 1904) figures two unusual instances of this condition. The first shows the extension of such fibres over an enormous area of the fundus, not only embracing the nerve in a complete circle about three disk diameters in extent, but also extending outward beyond the macula to a considerable distance, constituting in fact "by far the most conspicuous feature in the ophthalmoscopic picture." The disk itself, except for a small part of the lower and outer quadrant, was not involved. Another unusual feature was the absence of the lustrous appearance. The macular portion had, on the contrary, a dead-white character and

some irregularity of the surface. The eye appeared normal in other respects, but was totally blind without even perception of light, though it was not divergent and there was no nystagmus.

[Liebreich figures a very similar case in his atlas.—ED.]

In the author's second case an upward patch of about the usual size was completely separated from the disk by a clear interval of normal fundus, rather less than one-half disk diameter in width. This eye was healthy and had normal vision.

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**An Attempt to Estimate the Risk of Producing Sympathetic Ophthalmitis by Perforating Injury.**—BARRETT, England (*Intercolonial Medical Journal of Australasia*, January 20, 1904), after reviewing briefly some well-known figures bearing upon sympathetic ophthalmitis, concludes that the "risk of sympathetic ophthalmitis supervening in a case of a severe injury with iridocyclitis is certainly not less than 5 per cent. It is probably considerably more." He feels, after attempting to assess the value of these facts, more inclined than ever to emphasize the rule gradually formulated in practice that in general, and apart from exceptional circumstances, a hopelessly blind eye, which has been perforated at any time, should be excised.

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**The Subconjunctival Injection of Cocaine in Cataract and Other Operations.**—KOLLER, the discoverer of the anæsthetic properties of cocaine, remarks, in a paper read in the Section of Ophthalmology of the British Medical Association, which met at Oxford, July, 1904 (*The Ophthalmoscope*, September, 1904), that while cocaine was satisfactory in operations upon the superficial structures of the eyeball, it was disappointing in operations on the iris. To anæsthetize this membrane also, he practices, after a preliminary instillation of a mixture of cocaine and pilocarpine into the conjunctival sac, a subconjunctival injection—two to three drops—of a 5 per cent. solution at a point where the fixation forceps is to be applied. The injection must be subconjunctival, and not into the episclera, otherwise a troublesome œdema will occur which obscures the section.

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**A Case of Foreign Body Remaining in the Lens of the Eye for Six Years with the Lens Otherwise Clear.**—LEWIS (*Medical Record*, August 6, 1904) reports a case of a young man whose lens has contained a foreign body for the past seven years, with retention of full vision and full functional activity of the eye. The foreign body entered the lens through a small wound at the lower nasal part of the cornea. It can be seen in the lens as a dark, glistening particle, a little to the supratemporal side and slightly posterior to the equator. It was thought to be a piece of steel, irregular in shape and about 2 mm. in its largest diameter, a chip from using a chisel on a piece of steel. There was almost no reaction and the wound healed promptly. There were two attacks of what seemed to be conjunctivitis during the four months following the injury. There were no further ocular symptoms, and the lens has remained clear.

## OTOLOGY.

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UNDER THE CHARGE OF  
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ASSISTED BY

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**Uræmia, with Deafness as a Complication.**—DR. TREITEL (*Monatschrift für Ohrenheilkunde*, November, 1903), in the following case, had an opportunity to observe both blindness and deafness occurring in the course of uræmia incident to scarlet fever in a child, and to have a differential diagnosis satisfactorily confirmed. The patient was taken ill with scarlet fever on October 12th. Fourteen days later an inflammation of the ear supervened. On November 7th albumin appeared in the urine; the child became delirious, with a high temperature and rapid pulse, and convulsions and vomiting followed. Upon November 10th, one month after the onset of the illness, the hearing was entirely wanting, and the possibility of labyrinth implication was considered, but set aside in favor of the conclusion that the aural symptoms were of uræmic origin. On November 15th the hearing reappeared, and on the following day the vision was restored.

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**The Question of the Value of Paracentesis of the Drum-head.**—BUERKNER (*Archiv für Ohrenheilkunde*, August, 1904). In this paper the author, after citing authorities and defining the conditions under which paracentesis is presumably advisable in cases of acute suppurative inflammation of the middle ear, draws conclusions in favor of this procedure as contrasted with the occurrence of spontaneous opening, based upon his observations in 450 cases, in 300 of which he did paracentesis, the remaining 150 cases having come to him after the opening in the drum-head had been spontaneously established.

Of the paracentesis cases 76 per cent. were children and only 24 per cent. adults. The spontaneous perforations were more common in adults, 63.3 per cent. of these cases being children and 36.6 per cent. adults, the reason for this difference in the percentages in the two classes of cases being probably not so much the difference in the anatomical and pathological conditions as to the fact that in children the cases are brought to the notice of the surgeon at an earlier stage of the disease.

The proportion as to sex, in the paracentesis cases, namely, 6 to 4, was in accordance with the proportion of the sexes in all aural cases, 59.5 per cent. men and 40.5 per cent. women; while in the spontaneous perforation cases 55.4 per cent. were males and 44.6 per cent. females.

In an analysis of 200 paracenteses and 150 spontaneous perforation cases, of the former 172 healed within three days; there was recurrence of the inflammatory process in but 13 and mastoid complication in



but 1 per cent., while in the latter class 135 healed within three days; there were 26 cases of recurrence and 7.4 per cent. of mastoid complications.

The average duration of the inflammatory process, when paracentesis was done on the first day, was 7.6 days, when done on the second day 7.9 days, and when done later than the second day 8.6 days; where perforation occurred spontaneously on the first day the average duration was 17 days; on the second day the average was 24.7 days, and 26 per cent. of the spontaneous perforation cases became chronic.

In the paracentesis cases there was less subsequent disturbance of hearing than in the spontaneous cases, the proportion in the former being 3 per cent. and in the latter 12 per cent, the same advantage being shown for paracentesis in reference to the liability to recurrence of the disease, namely, but 8.5 per cent. in the former and 20.7 per cent. in the latter.

From these tabulated results of the observation of a limited number of cases, as well as upon the practical experience of over a quarter of a century, Buerkner concludes that in cases of otitis media with pain, swelling, or bulging of the reddened drum-head, and corresponding constitutional disturbances an early and free opening of the drum-head is the only rational procedure.

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**Contribution on the Surgical Cure of General Purulent Meningitis of Otitic Origin.**—MARCEL LERMOYEZ and LEON BELLIN (*Annales des mal. de l'oreille, du larynx, etc.*, tome xxx., No. 10) report two cases of purulent general meningitis of otitic origin cured by operation:

Case I. Female, aged nineteen years. For a year purulent discharge from the left ear, very abundant, fetid, at times tinged with blood, but without pain or disturbance of the general health. Later vague symptoms, headache, fatigue, and gastric disturbances. A few weeks later violent pains in the head, with vomiting. Signs of acute leptomeningitis, intense fronto-occipital headaches, pain on pressure upon the eyeballs. Slight left facial paralysis. Pupils equal, reacting to light. Fundus normal. Stiffness of the neck. Movements of flexion of the neck more difficult and painful than rotary movements. Patella reflex normal. Kernig's sign very marked.

Lumbar puncture: fluid transparent, under great pressure, containing lymphocytes, 58 per cent.; polynuclears, 40 per cent.; large mononuclears, 2 per cent.

*Operation.* 1. Mastoid opened at point of election: osteosclerosis of surface. Subcortical cells connecting with antrum filled with mucopus. 2. Opening of aditus and attic: middle ear filled with granulations, hammer carious, incus absent; facial nerve denuded at the level of the floor of the aditus to the extent of 5 mm. reddened, not œdematous, and could be raised from its canal. 3. Internal bony wall removed from level of roof of cavity, backward to the lateral sinus, which was intact without perisinal abscess. Dura thickened, covered with granulations, without perforation. A necrosed area of the inner wall of the middle ear without a fistula was apparent.

After operation the patient gradually improved. Lumbar puncture a week later showed: lymphocytes, 99 per cent.; polynuclears, 1 per cent.; fluid clear; headache was relieved; a fistula showed at the level of the aditus leading in the direction of the labyrinth. Another lumbar

puncture later showed a normal fluid. Two sequestræ were subsequently removed, the discharge ceased, the cavity epidermitized, and the patient was discharged well.

Case II. Otorrhœa from the right ear since infancy. Acute mastoiditis supervening, a petromastoid exenteration was performed. Eight days later there was acute general meningitis; the brain was then exposed and the exposure followed by incision of the dura mater and cerebral puncture. Four lumbar punctures were made within ten days; at each puncture ten to fifteen cubic centimetres of fluid were removed, which removal lessened the intense headaches and the stiffness of the neck. The pupils were unequal throughout the course of the disease.

Clinically, and by cytological examination of the cerebrospinal fluid, both of these cases were proven to be cases of purulent meningitis.

The writers conclude that the only complication of suppurative otitis which has baffled the surgeon, that is, purulent meningitis, may in the future be operated upon as successfully as the surgeon now operates in cases of brain abscess and sinus thrombosis. Four rules for the surgical treatment of purulent meningitis of otitic origin are then given, with detailed description.

Rule 1. Make a large opening of the middle ear and uncover the dura mater without going through it.

Rule 2. In case of failure of the preceding intervention, but in this case only, go through the dura mater in order to penetrate the sub-arachnoid space.

Rule 3. Practice and systematically repeat lumbar puncture.

Rule 4. Respect the labyrinth.

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**Practical Deductions from Our Recent Knowledge of Suppuration of the Labyrinth.**—DUNDAS GRANT (*Annales des mal. de l'oreille, du larynx*, etc., tome xxx., No. 10) is of the opinion that many cases of suppuration of the labyrinth have no doubt been overlooked, because they have not been thought of or not looked for. It is a new surgical field; Jansen and Brieger have shown the frequency of labyrinthitis as a cause of otitic meningitis, and Jansen, Okada, and Whitehead have evidenced its frequency as a cause of cerebellar abscess. Jansen found labyrinthitis in from 20 per cent. to 25 per cent. of his cases of radical operation on the mastoid.

*Prognosis.* When the petromastoid exenteration alone has been done the mortality has been about 50 per cent., but with operation upon the labyrinth also the mortality has been reduced to 20 per cent.

Besides meningitis, cerebellar abscess is another important cause of death in labyrinthine suppurations (12 per cent. to 33 per cent.), and a practical deduction to be drawn is that in cases of cerebellar abscess a labyrinth lesion, and not always a lesion of the sinus, may serve to explain the cause of the abscess.

To prevent labyrinthine suppuration especial care in the treatment of middle-ear suppurations, acute as well as chronic, should be taken. The longer they have been without treatment, the greater the chance of labyrinthine affection, and careful note should be taken in the course of middle-ear suppuration of increase of deafness, of decreased osseous perception, of disturbances of equilibrium, or of positive vertigo, especially when associated with nystagmus, headache, and vomiting. During mastoid operations the external surface of the labyrinth

should be carefully examined for local signs of labyrinthitis, to which end it is necessary to use powerful electric illumination, and hydrogen peroxide or adrenalin to stop bleeding; as much as possible of the posterior bony wall of the auditory canal should be taken away, and a rotating burr preferably employed to diminish concussion, especially in removing the hard external wall of the attic. The gouges used should be sharp and always directed obliquely to the bone. In a small number of cases it is impossible to introduce Stacke's protector between the posterior auditory canal and the external semicircular canal.

*Early Diagnosis.* (a) Before operation study the disturbances of equilibrium, which are more marked when the head is turned toward the diseased side; also nystagmus, which often only exists when the eyes are turned toward the well side. Make hearing tests with great care, Weber's test being often misleading in cases of labyrinthine disease. (b) During the operation examine carefully the external semicircular canal, the oval window, the round window, and that part of the cochlea at the level of the promontory; remove completely the external wall of the attic and the "spur." (c) After mastoid operation labyrinthine suppuration is to be suspected if headache, fever, vertigo, vomiting, or nystagmus persist, or appear. Note the similarity between symptoms of labyrinthine suppuration and those of cerebellar abscess, the points of difference most marked being in cerebellar abscess, slow pulse and respiration, low temperature, tendency to coma and drowsiness, cerebral torpor, constipation, and wasting. Disturbances of equilibrium are rare in cerebellar abscess, but very constant in the acute stage of labyrinthitis. The gait in cerebellar affections is comparable to that of a drunken man, while in labyrinthitis there is more subjective feeling of vertigo and a gait which Moos compares to that of a duck. The two affections may coexist; in fact, in half the cases of cerebellar abscess there is suppurative labyrinthitis also. Suppurative labyrinthitis may be latent; cerebellar abscess may have a long latent period.

*Indications for Operation.* In general, if there is pus in the labyrinth; severe labyrinthine symptoms unaccounted for or unrelieved by mastoid operation; presence, or threatening, of symptoms of meningitis, cerebellar abscess, cerebellar abscess or extradural abscess traceable to labyrinthine suppuration; if fistulæ and local signs of suppuration are found, in general if pus oozes, especially if it reappears after being wiped away.

*Remarks.* Evacuation of the labyrinth, unless necessary, adds to the risk of the operation. Suppuration is often limited to the external semicircular canal, a condition in which operation frequently leads to recovery. Inflammatory connective tissue in the internal auditory canal may prevent the suppuration from extending to the meninges. Nerve deafness may be due to a non-suppurative inflammatory lesion of the labyrinth. The openings of minute cells on the inner wall of the antrum should not be mistaken for fistulæ of the semicircular canal.

*Operation.* The best instrument, in the opinion of the author, is the rotating burr. Jansen, however, prefers the small chisels,  $1\frac{1}{2}$  to  $3\frac{1}{2}$  mm. in size. Sometimes it is impossible to avoid injuring the facial nerve. After opening the external semicircular canal the opening can be extended forward without difficulty into the vestibule. The burr may be used to enlarge the oval window inferiorly, and the cochlea may be opened with a very small burr in front of the round window.

## PATHOLOGY AND BACTERIOLOGY.

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The Islands of Langerhans in the Normal and Diseased Pancreas of Man, and Especially in Diabetes Mellitus.—SAUERBECK (*Virch. Arch.*, 1904, Bd. 177, p. 1) contributes a critical review of the literature dealing with the changes in the islands of Langerhans in disease of the pancreas and in diabetes mellitus, together with an anatomical study of the organ in health and under various pathological conditions. He estimates that the normal pancreas contains from three to ten islands in an area of 3.7 mm., the number varying a good deal in different parts of the organ. The islands in the interlobular form of chronic interstitial pancreatitis seem to be very resistant, while in lipomatosis of the pancreas without diabetes they may disappear to a considerable extent, though more frequently they are present in large numbers. The most remarkable resistance is seen in cases of carcinoma of the pancreas, in which condition they may remain entirely unaffected, even though considerable portions of the parenchyma are destroyed by the growth itself or by a secondary induration. In only 3 of 17 cases of diabetes mellitus was the pancreas extensively diseased. In eleven instances the organ showed either localized areas of sclerosis or a diffuse sclerosis of the interacinar type, lipomatosis, or other mild grades of alterations. In more than half the cases the islands presented some definite anatomical changes which were usually associated with disease of the parenchyma. The author, in summing up the results obtained by himself and by other observers, concludes that at least three organs must be kept in mind when considering the etiological possibilities of diabetes mellitus: the pancreas, liver, and nervous system. Experiments have demonstrated conclusively that complete removal of the pancreas is followed by glycosuria, while experiments and anatomical study have shown that provided the islands of Langerhans remain intact, practically the entire parenchyma of the organ may be destroyed without the occurrence of diabetes. Moreover, there has been no case of extensive disease of the islands reported without the presence of diabetes. If these facts speak for the "island theory" of diabetes mellitus, certain cases of suspected pancreatic diabetes that have been reported in which there was no disease of the islands seem to oppose it. In this latter group of cases the author believes that at least in some instances the diabetes may be dependent upon certain functional alterations of the islands not demonstrable with the microscope. He believes that in other instances the cause of the disease may be found in the liver or nervous system. He does

not consider that either functional or anatomical changes in the parenchyma of the organ are responsible for diabetes mellitus.

**On the Formation of Uric Acid in Gout, and the Causes of Its Precipitation in the Tissues.**—SCHMOLL (*Archiv. gén. de méd.*, 1904, t. ii. p. 2433), after discussing the formation of uric acid from nuclein, reviews the literature to show that neither the theory of retention nor the theory of increased production of uric acid in gout can be held to explain its presence in the serum of patients suffering from gout. The author rejects the theory of Roberts concerning the combination of sodium with the normal quadriurates in the blood, and advances the theory that under normal conditions the uric acid present is combined with thymic acid, the substance obtained when the xanthin bases are split off by oxidation from nucleinic acid. Thymic acid, then, is always present when uric acid is formed by oxidation. This method of formation Schmoll considers to be in operation during health. The combination of these acids cannot yet be detected. In gout, on the other hand, he considers the uric acid to be formed in part by synthetical processes, there being no production of thymic acid by this process. This absence accounts for the precipitable uric acid in the serum, which becomes deposited in the form of tophi. Two series of experiments in support of this hypothesis have been undertaken, the first to determine the influence of thymic acid on the excretion of uric acid, and the second to endeavor to obtain a proof of the synthetic formation of the uric acid in gout. In the first series it was found that administration of thymic acid to gouty patients greatly increased the amount of uric acid in the urine. This, the author considers, was due to the fact that the combination of uric and thymic acids takes place, and in this form the uric acid is much more readily passed into the urine. No such increase took place in normal individuals. The second series of experiments consisted in studying the constituents of the urine of a gouty patient under various diets. None of the changes of diet changed the amount of uric acid excreted in the urine, even though a diet free from nuclein bases was given. This the author considers can be explained only by assuming that uric acid is synthetically produced in the organism.

**Experimental Streptococcus Arthritis in Relation to the Etiology of Acute Articular Rheumatism.**—Although several English observers have recently done considerable work with the idea of isolating a specific organism pathogenic for rheumatic fever, their work has been done with very few or no control experiments.

R. I. COLE, in the *Journal of Infectious Diseases*, 1904, vol. i. p. 714, comments upon this fact and gives an account of his experiments with various strains of streptococci. The author obtained an organism from the blood of a patient during life, suffering from acute endocarditis which resembled culturally the ordinary streptococcus pyogenes, and which produced an arthritis in rabbits after intravenous injection. As the organism agreed quite closely with the so-called "micrococcus rheumaticus," Cole decided to use as control experiments streptococci isolated from various sources other than from patients with rheumatic fever. Six races of streptococci were used. These were obtained from peritonitis following carcinoma of the stomach; puerperal fever (autopsy);

blood during life in terminal septicæmia following myocarditis; empyema; blood during life in septicæmia following appendicitis; scarlet fever adenitis. The results of intravenous inoculation of these organisms into rabbits did not differ from those obtained in the experiments with the first organism from the case of acute endocarditis, nor did they differ in any marked degree from the experiments of those using the so-called "micrococcus" or "diplococcus" rheumaticus. Lameness was frequently produced, and, at autopsy, arthritis, from which lesions the organism could be regained, were frequently found. In 2 cases acute endocarditis was found at autopsy. One rabbit showed symptoms of inco-ordination similar to those that have been interpreted by other observers as chorea.

Colc concludes from these convincing experiments that arthritis and endocarditis may be produced by the intravenous inoculation of rabbits with streptococci from various sources, and the results obtained are quite similar to those described as resulting from the inoculation of the so-called "micrococcus" or "diplococcus" rheumaticus. He considers the description of a distinct variety or species of streptococci based upon the property of causing endocarditis and arthritis as unwarranted.

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**The Morphology of the Blood of Splenectomized Animals and of Animals with a Fistula of the Thoracic Duct.**—CRESCENZI (*Lo Sperimentale*, 1904, Anno viii. p. 547) has studied the quantitative and qualitative changes in the white blood corpuscles of the dog after splenectomy combined with the formation of a fistulous opening from the thoracic duct. In most of the dogs the flow of lymph ceased after twenty-four hours on account of thrombosis of the duct; one dog lived for five days with patent duct. The appearance of the lymph varied with the periods of digestion, at this time being much more milky than when digestion was not taking place. The lymph contained from 3000 to 7000 white cells per cmm., practically all of which were small lymphocytes. Examination of the blood of normal dogs showed that both the total numbers of red and white cells as well as the relative proportions of white cells varied between rather wide limits. The following numbers show the maximum and minimum limits of variations: red blood corpuscles, 4,940,000 to 8,360,000; white blood cells, 7830 to 16,780; eosinophiles, 5.8 per cent. to 1.4 per cent.; polymorphonuclear 65.5 per cent. to 85.5 per cent.; large mononuclears, 0.2 per cent. to 1.7 per cent.; small mononuclears, 5.8 per cent. to 33.7 per cent.; transitional forms, 2.1 per cent. to 17.5 per cent.

The experiments are divided into four groups.

- I. Simple exposure of the thoracic duct in cervical region.
- II. Splenectomy followed by fistulous opening into the thoracic duct one to two days later.
- III. Simple fistula of thoracic duct with free flow from central end.
- IV. Splenectomy and fistula of thoracic duct at same operation.

Immediately after all these operations, including the control experiments, the blood showed an elevation of the polymorphonuclear leukocytes. This change was thought to be dependent upon the effects of the operation *per se*. The small mononuclear lymphocytes dropped in the control experiments within one to two hours after the operation to about one-third of their original number, but rose again within twenty-four hours to a height equal or above that seen before operation.

In the other three groups of experiments the drop was much greater and lasted longer. Often the decrease was to four-fifths and occasionally ten-elevenths of the original number, even twenty-seven hours after operation. If at the same operation splenectomy was performed and a fistula of the thoracic duct made, the effect was most pronounced. This phenomenon was not lasting, however, for these cells gradually rose to their original numbers as in the control experiments. The large mononuclear cells and transitional forms did not show any constant change. Occasionally they fell, often rose, and sometimes made their appearance in the circulating blood where before they had been absent. Owing to the extreme fluctuations of the numbers of these cells in the normal dogs, no definite conclusions could be drawn as to the effect which the operations might have upon them. The eosinophiles decreased regularly in both the control and experimental dogs, and sometimes disappeared entirely from the circulating blood. Quite as regular was their reappearance and gradual increase. The author concludes that when either a fistulous opening is made in the thoracic duct alone, or this operation is combined with splenectomy, the circulating blood shows a temporary decrease in the numbers of small lymphocytes. This diminution is slight but constant, and is dependent upon the loss of lymphocytes brought to the blood by way of the thoracic duct. The subsequent increase of lymphocytes and final establishment of the normal numbers is not dependent upon a vicarious function of the bone-marrow to form lymphocytes, since a histological study of the bone marrow showed no evidence of lymphocyte production. Indeed, no difference could be made out between the marrows of animals killed during the period of greatest lymphopœnia and the most marked lymphocytosis. Neither could any compensatory flow of lymph into the blood from channels other than the thoracic duct be discovered. Crescenzi therefore concludes that the small lymphocytes enter the circulation directly from the lymph glands. The experiments seem to show further that all the white cells do not arise from the same hæmopoietic organ, and that the large lymphocytes and transitional forms are not derived from the lymph glands.

**Studies on the Pathological Anatomy of the Adrenals (Atrophy, Vicarious Hypertrophy, Tuberculosis).—**MARAKASCHEFF (*Ziegler's Beiträge* 1904, Bd. xxxvi. p. 401), after studying the adrenal glands in cases of Addison's disease, and in certain conditions in which the glands were the seat of marked pathological change, concludes that the cortical substance is particularly involved in cases of Addison's disease, and destruction of this portion may be followed by the entire symptom-complex. Moreover, the medullary substance may be completely destroyed without the presence of Addison's disease. If one adrenal is destroyed, an hypertrophy of the cortex of the other one may take place; this hypertrophy leads to great compression of the medulla.

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SYPHILIS OF THE LUNG:

WITH A REPORT OF THE ANATOMICAL FINDINGS IN A CASE.

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SYPHILIS of the lung is either congenital or acquired. In this paper only the latter form will be considered.

Whether we agree with the majority who hold that syphilis of the lung is rare in the adult, or with the few who consider it more common, we all must accept the opinion of the best authorities—that the condition does exist. Now, when it is taken into consideration that syphilis is curable and that the advanced cases of pulmonary tuberculosis, with which it is likely to be confounded, are, as a rule, incurable, one should be all the more careful to make no mistakes.

That syphilis of the lung is a very rare condition is almost universally conceded by men of large experience. Osler states that in twenty-five years he has not seen more than half a dozen specimens in which there was no question as to the nature of the trouble.<sup>1</sup> In 1898 the London hospitals and Royal College of Surgeons contained only ten specimens which seemed to be unquestionable examples of this disease.<sup>2</sup> Among 13,000 specimens in the Army Medical Museum at Washington there is not one of this disease.

There are others, however, who hold a contrary opinion. Porter considers it common in adults. Satterthwaite<sup>3</sup> thinks that lung syphilis is greatly underestimated by the general practitioner, and “almost unknown to many syphilographers.” Pankritius, Schnitzler, and Grandidier have also found it by no means unusual.

<sup>1</sup> Practice of Medicine.

<sup>2</sup> Fowler and Godlee. The Diseases of the Lungs.

<sup>3</sup> Boston Medical and Surgical Journal, 1891, vol. cxxiv.

Stengel<sup>1</sup> suggests that this difference of opinion depends largely upon the point of view of the observer—whether as a clinician or as a pathologist, the former believing that this condition is comparatively common, the latter that it is very unusual. It must be acknowledged that the pathologist has by far the best of it when it comes to producing convincing evidence. There is no disease, however, in which it is more necessary to carefully weigh the pathological findings with the clinical history before giving an opinion.

Without questioning their rarity, it may be well to mention one or two possible factors which have tended to reduce the number of cases reported. In the first place, it is most difficult to differentiate between pulmonary tuberculosis and pulmonary syphilis. This is well recognized, not only at the bedside, but in the pathological laboratory. In fact, the only absolutely certain point of difference in many cases is the presence of the tubercle bacillus, and even this unquestionable evidence of tuberculosis does not preclude the possibility of associated syphilis. Pulmonary tuberculosis is so common and syphilis of the lung thought to be so unusual that it seems probable that some of these cases, because of their very rarity, may slip by with a diagnosis of tuberculosis. Many cases of supposed phthisis give such a typical history and show such characteristic signs of the disease that it does not seem necessary to examine the sputum, or, even if the bacilli are not found after a few examinations, no change in the diagnosis seems called for. Satterthwaite<sup>2</sup> gives a very interesting example of such a case which fell into his hands and was subsequently cured by appropriate treatment.

The same line of argument is used in the post-mortem room. The condition is so much more likely to be tuberculous than luetic that it is almost always placed in that class unless pronounced syphilitic lesions of other organs are discovered.

**TERTIARY LESIONS.** While secondary lesions of the trachea have been occasionally observed,<sup>3</sup> there are, so far as I know, no records of such lesions in the bronchi. From the similarity of structure and function, however, there seems to be no reason why similar secondaries (mucous patches) might not be found, should an opportunity for their observation offer. The results of antisyphilitic treatment upon bronchitis occurring during secondary manifestations also serves to strengthen the theory of possible secondary bronchial involvement.

Tertiary lesions of the trachea and bronchi, consisting of gummatous infiltration of the submucous tissue, with consequent fibrous thickening and stenosis, are not unusual, and the lesions of the pulmonary parenchyma are solely of the tertiary type.

**THE PERIOD INTERVENING BETWEEN THE PRIMARY INFECTION AND THE APPEARANCE OF PULMONARY LESIONS.** Undoubted syphil-

<sup>1</sup> University of Pennsylvania Medical Bulletin, 1903-1904.

<sup>2</sup> Loc. cit.

<sup>3</sup> Morrell MacKenzie. Diseases of the Throat and Nose, London, 1880, vol. i. p. 510.

itic disease in the lungs has been recorded as early as one and as late as twenty years after the initial sore. The most usual time is, however, from the fifth to the tenth year after the infection. Frank<sup>1</sup> and Schirren<sup>2</sup> have reported cases only a few months after infection. My own case showed comparatively recent lesions twenty-one years after infection.

THE LESIONS OF SYPHILIS OF THE LUNG. 1. Gumma. 2. Pneumonia. 3. Fibrosis.

1. Gummata are either single or multiple, round, elliptical, or irregular in shape, and vary in size from a hemp-seed to a goose-egg, and in consistency from a soft colloid to a firm fibroid or cheesy tumor.

They may be found in any part of either lung, but are more usual within the substance and in the vicinity of the root, though they may be at the apex or upon the surface (my own case). Many observers claim that the right middle lobe is the favorite location. Grandidier<sup>3</sup> reported 30 cases in which the right middle lobe was the seat in 27. Hirsch<sup>4</sup> quotes Pankritius' statistics of 105 cases, in which 76 were right-sided, 18 left-sided, and 11 bilateral.

A gumma may present any of the following appearances, depending somewhat upon its age: It may be a gelatinous mass or a nodule of a grayish-white or yellow or reddish color, usually surrounded by a more or less distinct capsule, formed through inflammatory changes, set up in the surrounding lung tissue. On section there is a tendency for the centre to bulge somewhat, which is considered to be of some value as a distinction from tubercle, there being apparently more elasticity in the periphery of the gumma.

Microscopically they are found, like gummata of other organs, to consist of round cells, large spindle-shaped or irregularly formed cells, epithelioid cells, giant cells (though these are not as numerous as in tubercles), fibroid interstitial tissue, and elastic tissue. Councilman<sup>5</sup> considers the essential process in the production of gumma in the lung to be a pneumonia with fibrinous exudation, accompanied by fibrous change in the alveolar walls, the whole subsequently undergoing caseation. There is a tendency to caseation and degeneration, beginning at the centre; young vessels spring from the periphery and grow toward the centre, and lead to absorption of the caseous nodule. If the absorption is complete a cicatrix is formed. It is also believed by some that the broken-down material may be discharged through a bronchus, and thus a cavity may result. Cavity formation is, however, very rare. That the anatomical diagnosis of pulmonary syphilis is very difficult and sometimes impossible has been, and still is, the opinion of the most experienced observers (Virchow, Ziegler,<sup>6</sup> and Ribbert<sup>7</sup>).

<sup>1</sup> Wien. med. Presse, 1880, Bd. xxi. No. 38.

<sup>2</sup> Berlin. klin. Wochenschr., 1875, No. 15.

<sup>3</sup> Ueber die Syph. Erkrankung der Lunge, München, 1901.

<sup>4</sup> Johns Hopkins Hospital Bulletin, 1891, vol. ii., No. 11.

<sup>5</sup> Spez. path. Anat., 1898.

<sup>6</sup> Dermatol. Zeitsch., 1893-1894.

<sup>7</sup> Lehr. h. d. Path. Histol., 1896.

Dürck and Hektoen<sup>1</sup> believe that a distinction can usually be made by the presence of newly formed bloodvessels in gumma. Sometimes, even in quite necrotic areas, vessels may be seen. Tubercle, on the other hand, as is well known, never shows new blood cells, and those old ones which may have been caught in the growth soon become occluded by pressure or thrombosis.

It is impossible to distinguish between tubercle and gumma in some instances, except by the finding of the tubercle bacillus. In a general way it may be said that in gumma fatty degeneration plays a very important part, while in tubercle the hyaline form is the more usual, and that giant cells are much rarer in gumma than in tubercle.

The pulmonary tissue immediately surrounding a gumma is frequently found to be consolidated, and from this infiltrated area fibrous bands may be seen extending to other parts of the lung.

2. SYPHILITIC PNEUMONIA OF THE ADULT. It is pretty generally conceded that there is an infiltration of the lungs resulting from syphilitic infection, which alone, or in connection with nodules, may extend over a pulmonary lobe.

On section these infiltrated areas are of a dark slate or gray or grayish-red color, not granular.

Microscopically, as described by Aufrecht,<sup>2</sup> the alveoli were seen to be filled with cellular material, a few containing swollen alveolar epithelia exclusively; slightly more numerous were alveoli in which a small number of white blood cells were embedded in fibrinous masses, while the alveolar capillaries were distended with blood. But most of the alveoli appeared to be filled with small round cells interspersed with red blood corpuscles. A much larger quantity of the latter was present in the interalveolar and interlobular tissue. According to the same author, however, the only justification for considering this pneumonic inflammation as entitled to a special classification would be a considerable increase in the thickness in the walls of the smaller vessels.

3. FIBROID INDURATION. The proliferation of the connective-tissue elements may take the form of a thickening extending from the hilus around the bronchi and vessels, or of isolated masses of fibroid tissue in various parts of the lung, or of diffuse changes occupying the whole or the greater part of one lung.

This primary proliferation of the connective tissue in lung syphilis is considered by Pankritius<sup>3</sup> as being characteristic of lues, for, while in other diseases of the lungs which have a hyperplasia of the connective tissue, it is secondary to some primary condition, such as inhalation of dust, protracted croupous pneumonia, certain forms of tuberculosis, carcinoma, etc.

<sup>1</sup> Hektoen's *Trans. of Dürck's General Path. Hist.*

<sup>2</sup> Nothnagel's *Cyclopedia of Practical Medicine.*

<sup>3</sup> Hirsch, Jos. *Inaugural Dissertation, Munich, 1901.*

Microscopically this change is characterized by hyperplastic cellular proliferation of the interstitial, interalveolar, peribronchial, and perivascular tissues. The vessels show a thickening of the intima and the adventitia. The favorite seat of this form of the disease, as in the case of gummata, is said to be in the right middle lobe.

Virchow has pointed out that diffuse lung syphilis cannot be distinguished from the chronic pneumonia of stone-cutters and grinders.

**SYPHILITIC PHTHISIS.** *A Progressive Destructive Disease Due to Syphilis.* The possibility of such an entity as a result of syphilitic infection has not yet been satisfactorily proven. Osler says: "Personally, I have no knowledge of such an affection, either clinically or anatomically, and the cases which I have seen demonstrated do not seem to me to have characteristic distinction enough to separate them from ordinary tuberculous phthisis."

Until our knowledge of syphilis of the lung is much more exact than it is at present, we must agree with Fowler that before cases are put in this category they should fulfil the following conditions:

1. The cases must be complete—that is, the symptoms observed during life must be considered in connection with the lesions found on post-mortem examination.

2. The evidence of syphilitic infection must be undoubted.

3. Repeated examinations of the sputum must have been made, and the tubercle bacilli have been invariably absent, and the absence of tubercle from the lungs (as the cause of lesions) must be proved by post-mortem examination.

4. Syphilitic lesions about the nature of which there can be no doubt must be found in other organs. He gives several cases which seem to fulfil these conditions.

Of course, it is quite possible for a lobe or entire lung to be excavated as a result of more or less complete bronchial obstruction by a gumma, just as is occasionally seen in cases of aneurysm, but this is not due to the effect of the syphilitic virus upon the parenchyma.

It would hardly seem justifiable to classify separately certain changes observed in the bronchial glands and lymphatics in a case of syphilis of the lungs and other organs reported by Weber.<sup>1</sup>

**SYMPTOMS.** Cough is usually the first symptom to attract attention, but has nothing characteristic. It depends more upon the laryngeal, tracheal, and bronchial lesions than upon those of the lung proper; at least, until these have become serious.

There is in many of these cases an associated ulceration of the larynx, trachea, or bronchi, which causes more or less constant irritation, resulting in cough.

**Sputum.** At first the sputum is that of an ordinary bronchitis, but later may become fetid from the bronchiectatic cavities formed by

<sup>1</sup> Pathological Society Transactions, vol. xvii. p. 152.



the syphilitic changes in the lung. No tubercle bacilli are present in uncomplicated cases. There may, however, be elastic tissue depending upon the breaking down of the pulmonary parenchyma.

*Hæmoptysis.* This symptom, though not common, does occur, and is one of the most misleading, because it is so very usually a sign of tuberculosis (probably 5 out of 6 cases of pulmonary hemorrhage are due to tuberculosis). The amount of blood lost is not, as a rule, large, though a patient of Lancaux expectorated more than a litre in twenty-four hours.

*Dyspnœa.* This seems to be very usual. Of course, the frequently associated stenosis of the trachea and bronchi (pressure by gummata on cicatricial contraction) accounts for this symptom in many cases, but it sometimes seems out of proportion to the anatomical lesions. Mauriac explains its origin in these cases as due to flattening of the alveoli and degeneration of the alveolar epithelium. The shortness of breath is often paroxysmal and resembles at times bronchial asthma.

*Pain.* This is not considered an important symptom by the majority of observers.

**GENERAL SYMPTOMS.** *Fever.* The temperature is of no value for diagnostic purposes, as it may be high or fever may be absent entirely. When present it may be of the hectic type, as in tuberculosis.

*Night-sweats* have been noted, but are not so common as in tuberculosis.

*Emaciation*, though not as frequent as in phthisis, may, in advanced cases, be most pronounced.

**PHYSICAL SIGNS.** There is, unfortunately, nothing distinctive. The signs produced by consolidation, whether from gummata or infiltration of syphilitic origin, differ in no way from those of tubercles or tuberculous infiltration.

Bronchiectatic cavities or excavations in the parenchyma produce the same signs, no matter from what cause.

**DIAGNOSIS.** Some writers, especially the German, lay great stress upon the much greater frequency of syphilitic lesions in the middle lobe of the right lung. Grandidier, having observed this apparent preference in 27 out of 30 cases, considers it of the greatest importance in making a diagnosis. Schnitzler and Pankritius have made the same observation. On the other hand, Fowler<sup>1</sup> says: "A careful examination of undoubted specimens of pulmonary syphilis does not bear out the statement that lesions are generally limited to the middle part of the lung; they are so often found elsewhere that little importance attaches to the exact size in deciding the question of diagnosis."

A physical examination of the chest, taken with the symptoms,

<sup>1</sup> Loc. cit.

usually suggests tuberculosis, and this is the diagnosis made in the vast majority of cases. The absence of tubercle bacilli, after repeated examinations of the sputum, first suggests the possibility of syphilis. If a history of lues has not already been elicited, careful questioning may now bring it out, and a suspicion of the real cause of the trouble be aroused. The seat of the primary lesion may be found; the history of a cutaneous eruption, sore throat, or falling of the hair be given. Ulceration of the pharynx or larynx may be noted or probably luetic lesions of the bones, such as the sinking in of the bridge of the nose. Advanced arteriosclerosis in a young patient is also suggested. The signs and symptoms of stenosis of the trachea or main bronchi, where an aneurysm or growth can be excluded, may also strongly indicate syphilis as the probable cause.

**PROGNOSIS.** In early cases the prognosis is favorable. Unfortunately, a correct diagnosis is usually reached so late in these cases that the disease is many times too far advanced to admit of a cure. Whether antisyphilitic treatment will do much toward the removal of a gumma which is already in the advanced fibroid or cheesy state seems doubtful. The effect of treatment upon those chronic fibroid changes about the bronchi in the alveolar walls seems problematic in the extreme. The process may, however, be arrested. Bronchiectatic cavities are always serious, but when the obstruction is due to gummatous thickening, and not to fibroid contraction following submucous gummatous ulceration, it is probable that the condition may be cured; provided, of course, that it has not existed too long a time. If real cavity formation has occurred, the prognosis is unquestionably bad.

**TREATMENT.** Antisyphilitic treatment should be commenced without a moment's delay. The general trend of the present day is toward the use of mercury, as well as the iodides, in tertiary lesions, no matter where situated.

The administration of blue ointment by inunction and of potassium iodide by the mouth seems the best and most rapid way of combating this very serious disorder.

A great deal has been said about the occurrence of syphilis of the lung in conjunction with pulmonary tuberculosis. It may be said that it would seem the wisest plan, when such a condition is suspected, to institute the antisyphilitic treatment, with the hope of removing that infection at least. Cases have been reported which show that an antisyphilitic treatment may be carried out and the symptoms, such as roseola and ulceration of the pharynx, disappear without any ultimate bad results, so far as the tuberculous conditions are concerned.

The following report of a case of syphilitic disease of the lungs is of interest chiefly from a pathological point of view, as there were no symptoms which suggested the possible existence of the post-mortem findings:

William D., white, aged forty-four years; American; farmer. One uncle died of tuberculosis; otherwise the family history was good. He never drank whiskey and seldom beer; used tobacco moderately. At twenty-three years developed a sore upon the penis after exposure, the scar of which still remained. He received internal treatment at once and no secondaries developed. At thirty-nine years, sixteen years after the primary sore, he had a stroke, which paralyzed his right arm and the right side of his face. In about a year the paralysis was completely recovered from. Nine months ago he suffered from a swelling of the abdomen (probably ascites), for which he was treated and recovered.

For the past year he had been obliged to rise each night to urinate. For more than a month he had noticed that his feet were swollen, especially in the morning. Some months ago he ran a pitchfork into his ankle, making a small, punctured wound, which had never healed.

The present attack began, about two weeks before admission to the Garfield Hospital, with a cutting pain in the chest; a week later pain began in the abdomen. The feet and abdomen then became noticeably swollen, and there was dyspnoea on exertion. There was a cough with mucopurulent expectoration, which contained no tubercle bacilli.

The skin was pale, the eyelids puffy; there was general oedema. No thickening of the radials could be detected. The pulse tension was slightly plus. The heart was not enlarged; the second aortic sound accentuated; there were no murmurs. The respiratory sounds were harsh. The abdomen contained a fair amount of fluid. The thoracic and abdominal veins were distended. No enlargement of the spleen could be detected. The liver dulness seemed to be diminished, probably due to the floating up of the intestines by the ascitic fluid. The edge of the liver could not be felt.

Upon the sternum, between the junctions of the second and third ribs, was an irregularly shaped, flat swelling, which was not painful, giving to the examining finger a sense of hard elasticity. It was said to have followed a kick by a horse, and, as it was not recognized as a gumma, but little attention was given it.

The urine was scanty, averaging about 600 c.c. in the twenty-four hours. It was turbid, acid, specific gravity 1026, albumin two-thirds by bulk, no sugar; hyaline, fatty, granular, hyeloepithelial casts; a few leukocytes and blood cells. Ten and two-tenths grams of urea were excreted in twenty-four hours.

The urinary findings continued about the same through the course of the illness.

The blood showed 73 per cent. of reds, 8700 leukocytes, and 65 per cent. of hæmoglobin.

The oedema gradually became more pronounced, the ascites increased, and a left pleural effusion developed.

Treatment was of no avail, and the man died.

The clinical diagnosis was chronic parenchymatous nephritis, possibly of syphilitic origin.

I was present at the autopsy, which was performed by Dr. Butterfield. The notes read as follows:

Projecting from the sternum, between the second and third ribs, is an irregularly round nodule of firm consistence, not movable beneath the skin, about 3 or 4 cm. in diameter and 1.5 cm. in height. A pale, depressed scar, 1.5 cm. in diameter, on under surface of glans penis.

*Inguinal glands* enlarged and easily palpable. On the dorso-internal aspect of the left foot are two reddish areas covered with yellow crusts (scars from wounds mentioned in history).

Hypostasis in dependent portions. No evidence of cutaneous oedema. Parietal peritoneum thickened and opaque. Section of sternal nodule firm, yellow, surface smooth. It is firmly attached to sternum and adjacent ribs.

*Pleural membranes* thickened and opaque. Right cavity contains normal amount of fluid. Left cavity contains 45 to 60 c.c. of reddish serum.

*Left Lung.* Visceral pleura adherent at the apex anteriorly and posteriorly; also adherent between the lobes. On the anterior aspect of the upper lobe is a yellow nodule, 2.5 by 1.5 cm., adherent to the overlying costal cartilage. On section it appears to be encapsulated, extends down into the lung substance, is firm and is traversed by lines of pigment. The lung is crepitant throughout, slightly pale, and emphysematous along the anterior border and purplish-red at the base. Pigment deposits in septa; on section frothy serum exudes. Bronchi contain a mucopurulent material (cover-slip preparations show no tubercle bacilli). Weight, 505 grams.

*Right Lung.* Extensive adhesions at the apex, posterior portion of the upper lobe; also to diaphragmatic pleura. Pleura between the lobes adherent. On the inner aspect of the upper lobe is a yellow nodule, presenting the same general characteristics as that described in connection with the left lung. Lung crepitant throughout, pigmented pinkish. Bronchi contains mucopus. No tubercle bacilli demonstrable. Weight, 550 grams. No enlargement of the bronchial glands.

*Pericardium.* Parietal membrane thick, opaque. Cavity contains the normal amount of fluid. Heart apex is adherent at the base of the pericardial triangle. Epicardial membrane shows whitish opaque areas irregularly distributed over the heart. Myocardium thin, slightly flabby, and of a dark reddish-brown color. Aorta contains numerous atheromatous patches; on the aortic valve cusps are a few small vegetations. One leaflet of the mitral valve thickened and slightly contorted; the other slightly thickened. Other valves normal. Weight of heart, 241 grams.

Parietal peritoneum thick and opaque. Localized adhesions in some portions of visceral peritoneum. No excess of fluid. One large nodule in the omentum. No evidence of fat-necrosis.

*Liver.* Extensive adhesions to the diaphragm. Surface pale, marked by opaque, slightly depressed areas, a few mm. in diameter. Yellow encapsulated nodules in right lobe posteriorly. One extends into the liver substance for more than 3 cm. One very prominent nodule in the left lobe just at the fissure anteriorly. On section it is pale, firm, yellow, and showing a tendency to bulge in the centre of the nodule. Gall-bladder tense, with thick, greenish-black bile; not enlarged; no stones. Weight, 1668 grams.

*Pancreas.* Dense and enlarged; adherent to the spleen. Surface marked by numerous, whitish, opaque, miliary areas. Section firm; connective tissue between lobes increased and contains the same white opaque areas seen on surface of the viscus. Weight, 131 grams.

*Kidneys.* Right organ. Apex and adrenal body adherent to the liver; perirenal fat very abundant. Organ enlarged (12 x 6 x 4.3 cm.); surface smooth, pale, and mottled venæ stellatæ injected. Section showed no increased resistance on cutting. Cortex 9 mm. in width, pale, with yellowish areas. Pyramids congested, being of a dark purplish-red color.

Fat about the pelvis increased. Capsule strips readily. Weight, 293 grams.

*Left Kidney.* The same general characteristics as the right. Measurements, 13 x 6.5 x 4.5 cm. Weight, 294 grams.

*Spleen* enlarged, firm, but friable; surface smooth and capsule opaque. Section firm, deep red in color. Weight, 320 grams.

*Stomach and intestines* apparently normal. On the surface of the bladder there is a small nodule corresponding in consistence and color to those described in the liver, lungs, omentum, and upon the sternum.

**MICROSCOPIC FINDINGS.** The nodule upon the sternum showed the usual picture of a gumma.

Sections of the liver showed marked cirrhosis, gummata, and amyloid degeneration. The kidneys were the seat of a diffuse nephritis and amyloid change. The pancreas showed pronounced cirrhosis of the interlobular variety and areas of fat-necrosis. No sections were cut from the nodule in the omentum, nor from that upon the bladder, but the macroscopic appearance of all the nodules was the same, and I have no doubt that they were all gummata.

*The Lungs.* The two nodules described as being situated upon the anterior and inner aspects of the upper lobes of the right and left lungs, respectively, were found on section to consist of dense fibrous tissue, with necrotic centres (Fig. 1).

There was no distinct capsule on that portion of the growth toward the lung tissue. The alveoli seemed to fade so gradually into the

continuous fibrous growth that it was difficult to detect any distinct dividing line.

Numerous bloodvessels could be seen in the connective tissue (Fig. 2), and even a few in the necrotic area. This point is especially worthy of note, as it is considered by Dürck and Hektoen as characteristic of gumma in contradistinction to tubercle. The latter never show new bloodvessels. From the fibrous tissue of the nodule could be seen bands of connective tissue dipping down into the parenchyma of the lung, which in places showed a condition of catarrhal pneumonia (Fig. 3). On the outer aspect of the growth the fibrous tissue was continuous with the thickened pleura.

FIG. 1.

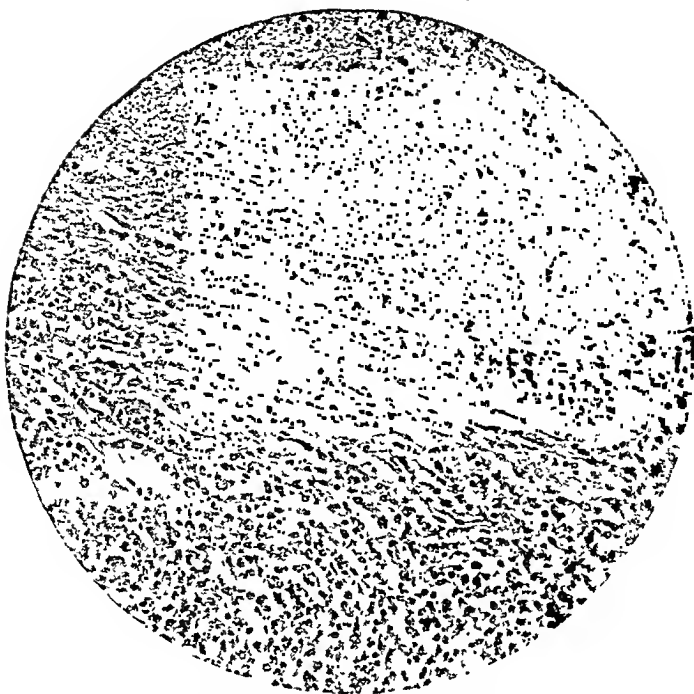


A section through part of a small gumma of the lung.  $\times 10$ .

A number of sections were made from both lungs, which showed irregularly distributed areas of fibrosis and also small areas of pneumonia. These consolidated areas were too minute to be detected macroscopically, nor could they be felt. There was a thickening of the adventitious coats of the arteries, but none of the intima. As to whether or not there was any actual increase of fibrous tissue about the bronchi, I was unable to convince myself; it was certainly not universal.

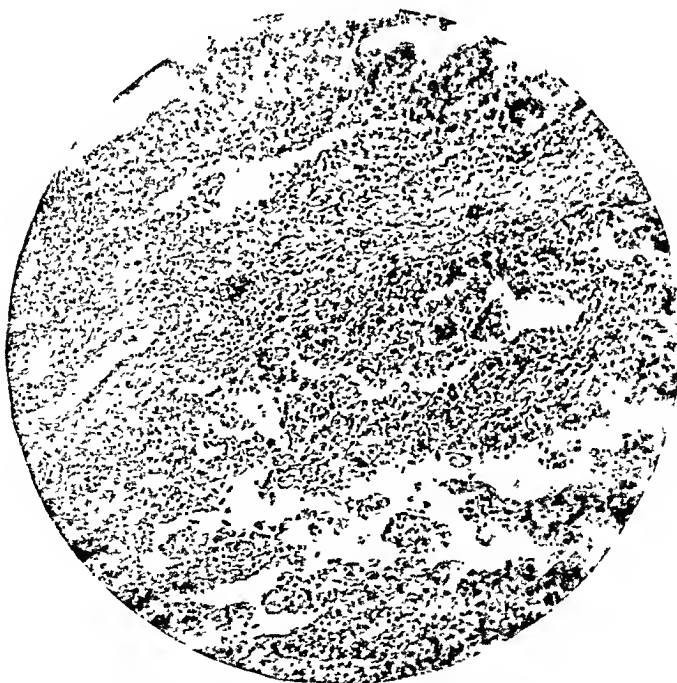
The belief that the nodules in the lungs were gummata is based on the following: 1. History of a chancre, the scar of which remained. 2. The history of a paralytic stroke at thirty-eight years. 3. The presence of undoubted gummata of the liver and on the sternum. 4. The absence of tubercle bacilli from the sputum before death and at post-mortem. 5. The absence of bacilli from the sections of the nodules. 6. Extensive amyloid change in the liver, spleen, and kid-

FIG. 2.



Showing part of the new-growth, with granulation tissue rich in capillary bloodvessels at the margin.  $\times 200$ .

FIG. 3.



Field beyond the fibrous area, showing a condition of catarrhal pneumonia and increased connective tissue in the area adjacent to the new-growth.  $\times 125$ .

neys. 7. The absence of any tuberculous involvement of the apices or any other part of either lung. 8. The presence of numerous bloodvessels in the new-growth.

Although the presence of considerable black pigment would suggest a possible cause for the fibrosis in the lungs, it was noted that the fibroid areas apparently bore no constant relationship to the patches of pigment, and, therefore, it seems fair to conclude that the scattered areas of fibrosis and of consolidation were also of syphilitic origin.

I wish to acknowledge my indebtedness to Dr. James Carroll for his aid and advice in interpreting the microscopic findings.

## SOME ASPECTS OF THE THEORIES OF IMMUNITY.

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ON infection by bacteria it is the bacterial toxins which cause disease, the bacteria as such merely representing inert foreign matter. There are two distinct classes of bacterial toxins:

1. *Extracellular toxins* secreted by the bacteria during growth. Such toxins dissolve out into the surrounding medium, causing disease and death by toxæmia. Examples, diphtheria and tetanus.

2. *Intracellular or endotoxins*, which can hardly be regarded as secretions, but rather as a part of the bacterial body substance, being only liberated on the death and dissolution of the bacteria.

In the latter case the bacteria on gaining entrance to the circulation or body fluids may be destroyed at once, the amount of toxin thus liberated being too small to affect the organism, or the bacteria may be able to multiply; progressive increase and destruction going on *pari passu* until the number being destroyed is so great that the intracellular or endotoxins are liberated in sufficient quantity to cause manifestations of disease. Radziewski<sup>1</sup> was the first to point out this principle in a clear and convincing manner. An infection by such bacteria may be circumscribed and express itself as a local inflammatory process or it may be generalized in the circulation, in which case it is called septicæmia or bacteræmia. It will be convenient here to speak only of bacteræmia. Examples: Typhoid fever, staphylococcus and streptococcus infections.

The processes of immunization against these two types of infection are entirely different:

1. In toxæmia antitoxins are formed which neutralize the toxin, but do not affect the bacteria.



2. In bacteræmiâ no antitoxins are formed against the intracellular or endotoxins, but means are adopted by the organism for destroying the invading bacteria.

It is the second of these processes which it is proposed to discuss here.

The antibodies formed in bacteræmia are the agglutinins, the precipitins, and the lysins or destructive agents.

The role of the agglutinins in immunization is very obscure. It was at first supposed that agglutinated bacilli are more easily attacked by the lysins than normal bacilli. But this notion has not stood the test of experiments, and there is no good reason to assume that bacilli are rendered more susceptible to the action of the lysins by the fact of being agglutinated.

Again, it has been suggested that the agglutinins help to prevent growth of the bacilli, holding them in check until the lysins can act, but experiments do not bear out this theory either.

If immune serum, say typhoid, is heated to 56° C. for thirty minutes, its lytic action is destroyed, but its agglutinating power is not affected. If such heated serum in a test-tube is inoculated with a loopful of a typhoid culture, the bacilli will grow very readily, although they are agglutinated as they grow. They grow in fact quite as quickly in heated immune serum as in heated normal serum; so it is obvious that agglutination does not retard growth, *in vitro* at any rate.

What assistance, therefore, the agglutinins render we do not yet know, and the same may be said of the precipitins, but the part played by the lysins is more obvious.

As an introduction to the subject Ehrlich's well-known theory may be briefly sketched; a theory which endeavors to explain the mechanism of the lytic action of blood. It will not be necessary to describe the experiments of himself and others on the results of which the theory is based.

**EHRLICH'S THEORY OF THE LYSINS.** *Normal Serum.* Normal serum is often strongly bacteriolytic for certain species of bacteria (typhoid, cholera, etc.).

The bacteriolytic action is due to two distinct principles acting in concert, the intermediate body (*Zwischenkörper*) and the complement. The intermediate body has an affinity for the bacillus, or rather for certain of the albumin molecules which go to make up the protoplasm of the bacillus, and enters into chemical combination with such molecules. The complement then enters into combination with the intermediate body and by virtue of its enzymatic nature can dissolve or destroy the albumin molecules of the bacillus to such an extent that the bacillus itself is destroyed.

It must always be borne in mind that the lysins are not directed against particular bacilli as such, but against certain albumins contained in the bacilli.

The complements exist in enormous numbers in the blood or fresh serum, but are of a very labile nature. On keeping serum for a few days the complements break up and disappear. Again, on heating fresh serum to  $55^{\circ}$  to  $56^{\circ}$  C. for thirty minutes the complements are destroyed. The intermediate bodies, on the other hand, are stable. They are not affected by keeping, even for months, or by warming until a temperature of about  $65^{\circ}$  C. is reached.

Serum from which the complements have been removed by keeping or warming to  $55^{\circ}$  to  $56^{\circ}$  C. is said to be *inactivated*. The intermediate bodies are still there and are able to attach themselves to the bacilli, but in the absence of the complements can exert no destructive influence upon them, and the bacilli grow freely in such serum.

The intermediate bodies are strictly specific—*i. e.*, an intermediate body which can combine with the albumins of the cholera bacillus is unable to combine with the albumins of the typhoid bacillus and *vice versa*. The complements, on the other hand, are not specific, although they may be multiple. Some may be better adapted for dealing with typhoid albumins, and others with cholera albumins, but there are probably many which can deal with various kinds of albumin indifferently. The question of the multiplicity or unity of complements, however, is still unsettled.

*Immune Serum.* On immunizing an animal to a bacillus, typhoid, for example, the complements are not increased in number. They remain numerically much the same as in normal blood, but the intermediate bodies for that particular bacillus multiply to an enormous extent, and are now known as *immune bodies*. It is not necessary to enter into the details of the mechanism by which Ehrlich accounts for the increase.

The immune animal, therefore, since its blood contains enormous quantities of immune bodies on account of the immunization, and enormous numbers of complements naturally, is able to dispose of enormous numbers of the particular bacillus to which it is immunized, although to other species of bacteria it is not, speaking generally, more resistant than it was in its normal condition.

This, in brief, is Ehrlich's theory, which, although leaving much yet unexplained, is the best concrete presentation of the subject that we possess so far, and is now very generally accepted.

Before proceeding to consider more in detail the lytic properties of immune serum, a digression may be made to point out that possibly the immunized animal is not more resistant to the action of endotoxins than it originally was in its normal condition.

A. Wolff<sup>2</sup> in recent articles has drawn attention to the analogy between bacterial endotoxins and the toxic principles of ordinary albumins. All inert albumins, when injected into an animal, are more or less toxic: red corpuscles, serum albumin, and egg albumen

very slightly; organ cells and especially spermatozoa more distinctly toxic.

Now, against the toxic principles of such albumins no immunity is conferred by repeated injections. On the contrary, the animal becomes more and more susceptible until it may succumb to a dose much smaller than would affect a normal animal. Moreover, the susceptibility is specific—*i. e.*, if an animal has become more susceptible to red cells, for example, it will resist an injection of spermatozoa as well as in its normal condition.

Agglutinins, precipitins, and lysins are formed against the albumins, but no antibodies which neutralize their toxic principles—*i. e.*, antitoxins. According to Wolff, the toxic principles of red corpuscles, spermatozoa, etc., are endotoxins, analogous to the endotoxins of bacteria. The endotoxins vary in the degree of their toxicity, but to all intents and purposes are similar in each instance, and no matter whether they are contained in the organ cells or in the bacterial cells, they are liberated on destruction of the cells and affect the animal organism in an analogous way. Since no anti-endotoxins are formed against them there is no increased resistance acquired on immunization. Some recent observations of my own seem to support these ideas of Wolff. Having had occasion to inject cancer extracts into rabbits, I found the animals stand the earlier injections, as a rule, very well, but soon lose flesh and often die after four or five infections, although the dose may be lowered rather than increased.

These rather sweeping statements of Wolff, however, cannot be accepted as proved. Although it may be taken for granted that no antiendotoxins are formed, it is usually supposed, and most experiments seem to bear this out, that some tolerance is acquired on repeated injections of organ or bacterial cells, just as tolerance to arsenic, nicotine, etc., may be acquired without the development of any antibodies.

It is generally accepted also that no antibodies can be formed against compounds simpler in structure than albumins, and this raises the question whether the endotoxins are actually of an albuminous nature or simpler substances against which one would not expect antibodies to be formed; a question which must be left undetermined for the present.

Whether the immunized animal is more resistant to the endotoxins than the normal is, therefore, still a moot point, but there is no doubt that a lethal dose *can* be reached in the immune animal by injections of large quantities of bacilli. In such a case the animal dies even though it may have destroyed every one of the bacilli injected (sterile death), so that at any rate the resistance to the endotoxins does not increase *pari passu* with the bactericidal power.

To return to the main argument we may take a rabbit, immunized to typhoid, and find that its serum can be inactivated at 56° C.,

mixed with living typhoid bacilli up to several times the lethal dose, and injected into the peritoneal cavity of a normal guinea-pig, or other animal, without injury to it. The immune bodies of the immune rabbit serum combine with the bacilli; the complements of the normal animal can now attach themselves to the immune bodies and, by dissolving out the albumins, destroy the bacilli. The immune serum can protect a normal animal against several lethal doses of typhoid bacilli. This may conveniently be called *passive* immunization as opposed to *active* immunization by inoculation with bacilli.

It is obvious that there is a minimum dose of immune serum which will protect. If there are not enough immune bodies injected to combine with all, or nearly all, of the bacilli, there may be more of the latter left alive than the normal animal can deal with on its own account and a fatal bacteræmia ensues.

So far all is plain sailing, but now difficulties begin to arise. The earlier experimenters, Löffler and Abel<sup>3</sup> in particular, observed that against typhoid bacilli not only is there a *minimum* dose of immune serum *below* which the serum will not protect, but there is also a *maximum* dose *above* which immune serum affords no protection. The accompanying table is given as an example. The injections were made into the peritoneal cavity:

TABLE I.

Immune serum and typhoid bacilli mixed and injected into guinea-pig. One loopful of bacilli is the minimum lethal dose (M. L. D.) per 100 grams of guinea-pig.

	Immune serum.	Bacilli per 100 grams of pig.	Result
1. Guinea-pig . . . . .	0 control	4 M.L.D.	Dies
2. " . . . . .	2 c.c.	4 "	"
3. " . . . . .	1 "	4 "	"
4. " . . . . .	0.5 "	4 "	Lives
5. " . . . . .	0.25 "	4 "	"
6. " . . . . .	0.1 "	4 "	Dies

The table only shows the principle, the amounts injected varying according to the strength of the immune serum and the virulence of the culture.

This was a phenomenon for which no explanation was forthcoming for some years after it was first observed.

In 1901 Neisser and Wechsberg<sup>4</sup> repeated these experiments, *in vitro*, and were able to demonstrate a similar occurrence by mixing immune serum with bacilli, adding a little fresh normal serum to supply complements (reactivation) and plating out. A table shows the results obtained by them better than explana-

tions. Each tube was made up to 2 c.c. by addition of physiological salt solution:

TABLE II.

	Typhoid immune serum inactivated at 56° C.	Emulsion of typhoid bacilli.	Fresh normal serum.	Colonies on agar plates made by taking five drops of mixture.	
				At once.	In five hours.
1 . . .	0	5 drops.	0.3 c.c.	Thousands	Thousands
2 . . .	1 c.c.	5 "	0	"	"
3 . . .	1 "	5 "	0.3 c.c.	"	"
4 . . .	0.5 "	5 "	0.3 "	"	Hundreds
5 . . .	0.25 "	5 "	0.3 "	"	0
6 . . .	0.1 "	5 "	0.3 "	"	Hundreds
7 . . .	0.05 "	5 "	0.3 "	"	Thousands

Neither the normal serum (1) alone at the dilution given, nor the immune serum (2) alone would kill any typhoid bacilli, but properly combined (5) they killed immense numbers. An excess of immune serum (3), however, is just as ineffective as too little (7).

These observations both *in vivo* and *in vitro* have been repeatedly confirmed and no one now doubts their correctness.

Neisser and Wechsberg's explanation is that the complements combine directly with the immune bodies, and this combination then attaches itself to the bacillus. If, then, the immune bodies are in excess of the complements, some of the immune bodies will be unprovided with complement, and these may attach themselves to some of the bacilli to the exclusion of the complement—immune body combinations. Such bacilli would escape unharmed, and, multiplying, set up a fatal bacteræmia.

This is called Neisser and Wechsberg's phenomenon or diversion of complements (Komplement-Ablenkung). Not only can complement diversion occur as explained, but it is also a fact that fresh immune serum alone *in vitro* will often not kill its specific bacillus. The following table gives an example from among my own experiments:

TABLE III.

Fresh rabbit serum eighteen hours old; 1 c.c.	Bacilli.	Number of bacilli per cubic millimetre estimated from colonies on agar plates.		
		At once.	In five hours.	
1. Normal.	Typhoid.	1000	0	The bacilli have been killed.
2. Serum of same rabbit after immunization to typhoid.	Typhoid.	1000	2000	The bacilli have multiplied.

This is probably another instance of complement diversion.

We find, then, that immune serum may not kill its own specific bacilli *in vitro*, and that an excess of immune serum may not protect a normal animal. In the latter case there must be complement diversion *in vivo*, yet if we take an immune animal and inject large quantities of the bacilli of immunization the bacilli are always destroyed; so it does not seem that there can be any complement diversion in such cases.

The destruction may even be on such an extensive scale that the immune animal is actually killed by the endotoxins liberated. Why should there be complement diversion in the case of the passively immunized, and apparently none in the case of the actively immunized animal?

Consideration of this question will entail a rather lengthy discussion, throughout which the main point must be kept in view or the thread of the argument will be lost.

Is it possible that in the immune animal itself the complements are locked up in some way so that they cannot combine with the immune bodies until after these have become attached to the bacilli? Supposing, for instance, as Metchnikoff<sup>5</sup> holds, that in the ordinary way the complements are contained in the leukocytes and not liberated at all, the bacilli becoming loaded with immune bodies and then taken up by the leukocytes, which digest them by virtue of the complements which they contain.

Metchnikoff's theory can now be taken up to see if it will help to solve the difficulty.

Metchnikoff's original idea, derived from observations on *Daphnia* and other lower organisms, was that it is the polynuclear leukocytes alone which destroy bacteria by means of phagocytosis. This is the purely cellular theory as opposed to the purely humoral theory that the bacteriolytic agents only exist free in the blood plasma or serum. When it was proved beyond all doubt that the immune bodies and complements do exist free in the serum, of vertebrate animals at any rate, Metchnikoff had to modify his views. He now admits that the immune bodies are secreted and dissolved out into the blood plasma, probably by the leukocytes, though possibly by other cells also. But the complements (his cytase) are formed by and retained within the leukocytes, and are only liberated on injury to or death of the latter. The complements do not normally exist free in the blood or body fluids.

The immune bodies, therefore, are analogous to the extracellular toxins and the complements to the endotoxins of the bacteria.

Metchnikoff bases this theory mainly on certain experiments made under his direction by Gengou,<sup>6</sup> who drew blood into paraffined tubes, centrifugalized quickly before the blood coagulated, and drew off the plasma. The plasma so obtained was much less bactericidal than serum obtained in the ordinary way. If the

blood is allowed to clot and the serum drawn off, there is destruction of leukocytes and the complements are liberated. If the plasma is taken by Gengou's method there is no or very slight destruction of leukocytes; so the plasma is not at all or very slightly bactericidal. Proof 1.

Again, Gengou found that leukocytic extracts, obtained by injecting starch suspensions into the pleural cavities of dogs or rabbits and withdrawing the sterile exudates, were strongly bactericidal after keeping for twenty-four hours at 37° C. Many of the leukocytes have perished and liberated the complements. Proof 2.

Now, experiments with immune animals are usually made by injections into the peritoneal cavity. In such cases, says Metchnikoff, the injection of comparatively large amounts of fluid causes *phagolysis*, or destruction of leukocytes, so that complements are set free and the bacilli killed, extracellularly at first to some extent, but in a short time fresh leukocytes arrive which take up the bacilli still remaining, now loaded with immune bodies, and complete the digestion by means of the complements (cytase) contained in them.

Metchnikoff, who, be it said at once, is not arguing all this as an explanation of the difficulties of explaining complement diversion, therefore takes us almost back to the purely humoral theory, and has to admit that destruction of bacteria may occur extracellularly *in vivo*, as well as in the interior of the leukocytes. Still, he lays great stress on the importance of phagocytosis, and we may suppose that after the primary extracellular destruction of bacteria, during which there may be some diversion of complements in both the actively and passively immunized animal, the phagocytes in the former case arrive more promptly and are more active than the phagocytes of the passively immunized animals. That the phagocytes in the *blood* of an immune animal are more effective than those of a normal animal will be shown later. Consequently the bacilli which have escaped extracellular destruction on account of complement diversion are taken up by the leukocytes later on: *in toto* by those of the actively and only partially by those of the passively immunized animal.

For this reason, although there may be an excess of immune bodies and some complement diversion in either case, the actively immunized animal lives and the passively immunized one dies.

In the animal or patient, self-immunized on account of natural infection, there would be no destruction of leukocytes, and, therefore, no chance for diversion of complements, since these would not be liberated.

This, however, is not a very satisfactory explanation and becomes of doubtful significance when we find it quite possible that Metchnikoff has based his conclusions upon erroneous premises.

1. EXPERIMENTS WITH PLASMA. Although a great number of observers agree with Gengou that plasma is less bactericidal than

serum, there are many who deny this. Vedder,<sup>7</sup> to mention one author, followed Gengou's methods very closely, and came to the conclusion that the plasma so obtained was just as bactericidal as the serum, no more and no less. It is, therefore, by no means certain that the complement content of serum is due to destruction of leukocytes during clotting.

2. LEUKOCYTIC EXTRACTS. Gengou's method of obtaining leukocytic extracts was as follows: He drew the leukocytic exudate from the pleural cavity and centrifugalized. The fluid above was then drawn off, the leukocytes washed twice, allowed to stand for twenty-four hours at 37° C., and then again centrifugalized. The clear fluid drawn off from above the washed leukocytes was bactericidal. Ergo, the complement had been liberated from the leukocytes as they disintegrated. The accuracy of this observation has also been challenged. Petrie,<sup>8</sup> for example, working with an improved technique, washed the leukocytes four times, and then ground them to pieces at the temperature of liquid air, —180° C. The extracts so obtained were not in the least bactericidal, nor would they reactivate inactivated immune serum, as complement-containing serum will do.

Therefore, he decides that the leukocytes do not contain complement, a conclusion directly opposed to that of Gengou. Petrie points out three sources of error in Gengou's methods:

(a) The leukocytes were only washed twice. If Petrie only washed twice, his extracts were somewhat bactericidal. This was because the complement-containing fluid portion of the exudate had not all been washed out. The fact that the partially washed extracts were bactericidal also shows that the low temperature of —180° C. is not injurious to complements.

(b) Complements are very labile, and keeping at 37° C. for twenty-four hours would weaken them considerably.

(c) When cell suspensions are kept at 37° C. for twenty-four hours they will undergo some self-digestion (autolysis). Now, Conradi<sup>9</sup> has shown that fresh organ extracts, liver, spleen, etc., are very slightly, if at all, bactericidal, but after a short period of self-digestion they become markedly so, not on account of increase of labile complement, but of stable basic products of the autolysis.

Petrie, therefore, decides that if the bacteriolytic action of Gengou's extracts was due to complement, it was because the fluid of the exudate had not been thoroughly washed out. But in all probability it was not due to complement at all, but to basic products of autolysis.

Petrie's contribution is undoubtedly of great importance and shows that at the best we must accept Gengou's conclusions with considerable reserve. It cannot be taken as proved that leukocytes contain complement which is liberated on their disintegration.



Careful experiments by several recent observers, notably A. Wolff,<sup>10</sup> show, that on injection of bacilli into the peritoneal cavity of immune animals, the bacilli are all destroyed extracellularly in a very short time, before the arrival of the leukocytes. These come in later, nevertheless, but there is *nothing left for them to do* except to carry off the remains. There seems to be little doubt that this is the case.

Again, the later experimenters have been quite unable to demonstrate that there is any phagolysis on injection of fluids or suspensions of bacteria into the peritoneal cavity; so it is very doubtful if Metchnikoff is justified in asserting that phagolysis occurs.

Phagocytosis, therefore, according to A. Wolff and others, plays only a secondary part in bacteriolytic phenomena, and is altogether absent in the peritoneal cavity of the immunized animal.

Seeing to what an extent various authors differ in their views, we must hesitate to accept one theory to the exclusion of others, although so far as the peritoneal cavity is concerned it seems most probable that the role of phagocytosis is comparatively unimportant. The latest and most careful observations tend to support this view.

Although we cannot attempt in the present state of our knowledge to explain by experimental evidence why diversion of complements occurs *in vitro* and in passively immunized animals, while in actively immunized animals apparently no such diversion takes place, yet we must remember that once blood is shed the condition for bacteriolytic processes are artificial, and it is quite possible that in the serum the affinities of the immune body and complement are increased so that they will combine more readily than in the immune animal itself. If this is so it would account for the phenomena observed. But it is pure hypothesis. There is no experimental proof of it.

In any case the peritoneal cavity is not an ideal spot to gain information about infection and immunity. The fight between the organism and the bacteria goes on for the most part in the circulation if the infection is general. The blood, therefore, is likely to afford a better insight into the processes involved, and within the last two or three years a new school has arisen—the opsonic school of Wright, as it may be called from its founder, which bases its theories mainly on observations of what appears to go on in the blood.

In 1902 Leishman<sup>11</sup> published a method by which the phagocytic action of leukocytes may be observed *extra vitam*. He takes a drop or two of blood, mixes it with an equal quantity of an emulsion of bacilli on a slide, and puts a cover-glass on it. The specimen is allowed to stand for thirty minutes in the incubator and then a smear is made and stained. The polynuclear leukocytes are seen to contain bacilli; those of normal blood a few; those of immune blood a large number. We may suppose, for instance, that the

average number of bacilli in each leukocyte of normal blood is four or five. It is found that in a parallel experiment made with immune blood the number may average fifteen to twenty in each leukocyte.

Wright<sup>12</sup> and Bulloch<sup>13</sup> have made extensive observations on this phenomenon and have come to the conclusion that there is some principle, opsonine (feast preparer), in immune blood which enables the leukocytes to take up and digest the bacilli more readily than normally. This principle resides in the serum, for if the leukocytes of the immune blood are washed free of serum with salt solution they are unable to take up any quantity of bacilli; not more can be taken up by the leukocytes of normal blood.

The opsonine, so far as has been determined, does not destroy the bacilli extracellularly; so its action is not analogous to that of the complements and immune bodies, but, like the latter and the agglutinins, it can attach itself to the bacilli.

For instance, if on the one hand bacilli are treated with immune serum, washed free of serum, and suspended in salt solution, while on the other hand leukocytes are washed and suspended in salt solution, the two suspensions can be mixed, and the leukocytes will take up the bacilli now loaded with opsonine just as freely as in immune blood. Wright does not enter into the question of the relations between opsonine and the lysins. This is left undetermined for the present, but we may consider it probable that whatever may go on in the peritoneal cavity, in the blood phagocytosis must play a leading part, and the latterly somewhat discredited phagocytic theory of Metchnikoff may obtain a renewed lease of life from a new point of view.

**THERAPEUTICS IN BACTERÆMIA.** While the principles involved in the foregoing discussions are of great theoretical interest, the ultimate object of research work in this field is to find some therapeutic agent for bacteræmic infections.

The success of the antitoxin treatment of diphtheria led to the hope that all bacterial diseases might be beneficially treated with antiserums. With this idea in view experiments were made on a large scale with antityphoid, antistreptococcus, antipneumococcus, and other antiserums, but with little or no success.

The reasons for failure are not far to seek. Such serums contain no antiendotoxins, so would not neutralize the endotoxins, although they would assist bacteriolysis if injected into a normal animal together with their specific bacterium. If used on a patient, however, the serum would be taken from stock in hand and, therefore, not fresh, so that the complements would have disappeared, leaving only the immune bodies. But the patient's blood is probably already loaded with immune bodies, so that the injection of a further quantity could do no good and might do harm if there were any tendency to diversion of complement, owing to intro-

duction of artificial conditions. It does not seem likely that any such antiserums will ever be of use.

Suggestions have frequently been made that to inject the fresh complement containing serum of an animal might lead to good results. In all probability, a typhoid patient, or one suffering from an analogous infection, has an excess of immune bodies and a deficiency of complements in his blood, and by supplying more of the latter the bacilli could be destroyed more rapidly. It is by no means certain that this would be the case, but, granting that it is so, an element of danger may arise. On sudden destruction of large numbers of bacilli, such as might occur on injecting a large number of complements, endotoxins may be liberated to such an extent as to cause an aggravation rather than an abatement of the fever or other symptoms, or even lead to the death of the patient.

In the present state of our knowledge the dosage of complements would be altogether empirical. The complement content of serums varies so much that it would be impossible to estimate the amount of complements injected at any one time, nor could one judge of the quantity required to do good without introducing the element of danger.

VACCINES. Wright claims that the opsonic power of the blood can be increased by injections of killed cultures (vaccines), and has treated several cases of carbuncle, resulting from staphylococcus infection, with apparently beneficial results.

The cultures of staphylococcus are killed at a temperature of 60° C. and the sterile suspension injected into the patient. The serum of such patients may not, and usually does not, kill one single staphylococcus *in vitro*, but examination of the blood by Leishman's method before and after injection shows that the power of the leukocytes to take up the cocci is very greatly increased. Coincidentally with this increased opsonic power of the blood the patient improves in health. The same has been observed with tuberculous patients after injection of tuberculin.\*

Wright<sup>14</sup> has also used this method as a prophylactic against typhoid fever and has succeeded in standardizing the dosage of vaccine with considerable accuracy. As a result of two or three injections into a healthy subject the opsonic power of the blood for typhoid bacilli is notably augmented and it is inferred that this indicates an increased resistance to infection.

During the Boer War Wright's vaccines were largely used among the British soldiers, but statistics, more or less carefully kept, did not bear out the claims of the originator for the treatment, and it has been abandoned by the war-office authorities.

Wright intimates that it was the statistics and not the treatment which were at fault. However this may be, it seems likely that

\* Lancet, October 10, 1904.

future prophylactic and curative measures against bacteraemia will be along the lines of vaccines rather than antisera, yet in all probability a considerable period must elapse before the bacteriologist will be of much assistance to the clinician in his treatment of such infections.

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## RECURRENT OCULOMOTOR PALSY, WITH A REPORT OF A CASE.<sup>1</sup>

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RECURRENT oculomotor palsy is a rare affection, although cases have been reported in this country by de Schweinitz,<sup>2</sup> Leszynsky,<sup>3</sup> Sachs,<sup>4</sup> Weber,<sup>5</sup> and Onuf.<sup>6</sup> The reports in most of these cases have been very brief, and it is doubtful whether, according to the distinctions of Möbius, most of these cases should be regarded as typical. The following case should be classed in the symptom group.

On October 31, 1904, C. C. N., a physician, aged thirty-one years, consulted one of us (Dr. Posey) on account of double vision and drooping of the right lid. His eyes had been refracted five years previously, while he was in attendance at the medical school, because of recurrent attacks of pain in and over the right eye, but nothing abnormal in the eye grounds or in the extra-

<sup>1</sup> Read before the Ophthalmological Section of the College of Physicians of Philadelphia, December, 1904.

<sup>2</sup> Boston Medical and Surgical Journal, 1895.

<sup>3</sup> Medical Record, May 25, 1901, p. 812.

<sup>4</sup> Journal of Nervous and Mental Disease, 1901, p. 462.

<sup>5</sup> *Ibid.*

<sup>6</sup> *Ibid.*

ocular muscles had been noted at that time. The patient still wore the glasses which were then given him for the correction of a moderate amount of hypermetropic astigmatism, and which for a time had relieved his symptoms perfectly. When the eyes were examined for the purpose of ascertaining the cause of his present difficulty, an almost complete ptosis of his right upper eyelid was at once manifest, while further study elicited that the inferior oblique and the internal rectus muscle of the same eye were paretic. The upper lid and the extraocular muscles of the left eye were unaffected, and the irides and ciliary muscles acted normally in both eyes. Corrected vision was also normal in both. An examination of the nose and its accessory sinuses by Dr. Freeman revealed nothing abnormal.

The diagnosis pointed to a partial palsy of the external division of the-right oculomotor nerve; upon questioning the patient, however, in order to ascertain the cause of the palsy, a series of facts was developed which at once surrounded the case with unusual interest and indicated that the character of the affection was quite out of the common. The family history of the patient was good, his father being still alive at the age of seventy-five years; his mother having died of splenic anæmia when forty-nine years of age. Four brothers and one sister are living and well, one brother having died of acute pancreatitis at thirty-six years of age. There is no history of nervous or neurotic disease in the family, nor, as far as the patient could ascertain, had any of the members been the subject of an ocular palsy. His sister is rheumatic and suffers from migrainous attacks, but all his brothers are free from them.

In early childhood the patient had measles and had repeated attacks of lumbago, which have persisted with a moderate degree of severity until the present time. When he was about fourteen years of age he began to suffer from spells of dimness of vision, associated with flashes of light upon the side, and followed by headache and nausea. These seizures apparently were typical attacks of migraine. They occurred upon both sides of the head and were brought on by gastric disturbances, overuse of the eyes, and general fatigue. At the end of two years the character of the attacks changed as the spectra disappeared, though the pain in the head and the gastric symptoms still persisted. While in attendance at the medical school, the pain in the head was almost constantly present, especially over the right eye, which led him, as mentioned above, to seek relief from glasses. His health is otherwise good and gonorrhœa and syphilis are denied.

In January of this year, after continuous professional work of more than usual severity, following an attack of pain in the right eye which had persisted for a few days, he saw double for the first time. He is unable to say whether the attacks of migraine had been more aggravated just prior to the attack of diplopia than usual, but he is confident of the preceding pain in the eye without

the migrainous symptoms. At the time of the attack the double vision was more marked when he looked to the left and above, but there was no ptosis. This diplopia persisted several weeks and

FIG. 1.



Left eye fixing an object above. Right eye is deviated downward, and the lid is drooping.

FIG. 2.



Left eye fixing an object far to the left and slightly above the horizontal visual plane. Right eye is deviated down and in, as a consequence of a paretic condition of the right inferior oblique and internal rectus muscles.

then gradually passed away, leaving no apparent ocular disturbance, his eyes giving him no further trouble until July, when a return of the double images was again remarked. The double images were of much the same character as in the preceding attack, but there was the additional symptom of the drooping of the upper lid of the right eye. At first the ptosis was intermittent, but in the course of a few weeks it became permanent and almost complete, until November 1st, when the lid raised for several days, but dropped again, however, and the eye remained closed until November 24th, when the lid again raised and resumed its natural appearance and so continued one week, when it began to partially droop, in which condition it still remains.

On account of the unusual course of the palsy, the attack of diplopia six months previous to the onset of the present palsy being also occasioned in all probability, as judged by the position of the double images, by an involvement of the right oculomotor nerve, it was thought best to ascertain whether there existed any further involvement of the nervous system. The patient was accordingly examined by one of us (Dr. Spiller), who found that he closed his eyelids well, drew up the corners of the mouth fairly well together, but not very well separately. The tongue was protruded straight, was moved freely, and showed no fibrillary tremors. The masseter contracted well on each side. Sensation for touch and pain was normal in the two sides of the face.

He had no weakness of the limbs. The patellar reflexes were prompt but not excessive, and the right was a little prompter than the left. The Achilles jerks were prompt but not excessive, and he did not have ankle clonus. Sensation for touch and pain was normal in the hands and feet. The gait and station were normal with eyes open or closed. He had possibly an area of slight hypalgesia on each side of the thorax about the nipple line; this, however, was not positive, and tactile sensation here was normal.

The patient when questioned gave further information regarding the attacks that he had had when he was about fifteen years of age and later. In these he would become completely blind, and would not recognize an object across the room, although he could see light faintly. These attacks lasted about half an hour, and were followed by severe headache. During the blindness he saw flashes of light. The blindness disappeared before the headache developed. He had not had any of these attacks during the past ten years.

Möbius gives a description of recurrent oculomotor palsy somewhat different from that of most writers. He presents a brief summary of all the cases reported since 1895, but of these only 6 are regarded as typical. They are the cases of Karplus (3), de Schweinitz, Ballet, and Paderstein. The symptoms begin in youth, at least before the twenty-fifth year. There is no heredity and the patients do not usually come from families in which migraine

occurs, although the occurrence of migraine in the family is not sufficient to prevent a diagnosis. The attacks always begin with headache, vomiting, or nausea, and, as a rule, the headache ceases when the paralysis develops, but it may last a few days after the paralysis has begun. There may be vertigo, increased flow of saliva, and vasomotor symptoms. Flimmer scotoma does not occur. The paralysis never develops without migraine, but there may be attacks of migraine without paralysis, and the headache is always on the same side. The migraine may last hours or weeks; the paralysis weeks or months; indeed, the headache is likely to last longer than in the simple migraine. The frequency of the attacks varies, there may be several attacks in one year, or several years may intervene between the attacks, but there is a type for every case. The periodicity is like that of epilepsy, migraine, and periodic insanity. The oculomotor paralysis is unilateral and complete, never confined to the external ocular muscles, or to the internal. Between the attacks some weakness of the oculomotor supply persists, and in course of time the residual paralysis increases. The first branch of the trigeminus has been found implicated.

Möbius combats Charcot's opinion that the periodic oculomotor palsy is a form of migraine (*migraine ophtalmoplégique*), and he believes the migraine is only symptomatic, as it may be in epilepsy or parietic dementia. Migraine may cause oculomotor palsy, but in periodic oculomotor palsy the lesion causes the palsy and the migraine is an aura. How migraine may cause the palsy is unknown. In most cases of periodic oculomotor palsy the paralysis occurs in the first attack.

Möbius<sup>1</sup> assumes that the lesion is at the base of the brain. He mentions that de Schweinitz has reported recurrent abducens palsy.

Oppenheim<sup>2</sup> gives a more liberal interpretation to the symptom-complex. According to him the periods may be irregular, all the oculomotor supply need not be implicated, and the paralysis may be confined to one muscle, as the levator palpebræ superioris in Knapp's case. The second branch of the trigeminus may be affected. In the intervals between the attacks there may be no paralysis. In the cases in which a necropsy has been obtained (Ziehen, Weiss, Thomsen-Richter, Karplus) basal hemorrhagic pachymeningitis was found in one case, a tubercle, a fibrochondroma, and a neurofibroma in the others. Oppenheim thinks that the periodic oculomotor palsy is related to migraine, as Charcot believed, and dependent upon vasomotor disturbance. Spasm of the vessels obstructs the blood supply and causes the paralysis, or overfilling of the vessels compresses the nerve. Attacks may occur without permanently injuring the nerve, but finally degeneration

<sup>1</sup> Deutsch. Zeitschrift f. Nervenheilkunde, 1900, Bd. xvii. p. 291.

<sup>2</sup> Lehrbuch der Nervenkrankheiten, third edition.



and inflammatory changes occur in the nerve and the paralysis persists. Such vascular disturbances may cause exudative processes or tumor. The symptoms may be progressive, or may be arrested, or may disappear.

Some very important distinctions will be noticed between the descriptions of Möbius and Oppenheim. A lesion may readily cause a paralysis of only certain branches of the oculomotor nerve, even though it be a tumor at the base, and a partial palsy should not be sufficient reason for exclusion of a case. The limitation to an age below twenty-five years is certainly arbitrary.

The case that we have studied is especially interesting in regard to the migrainous attacks. When about fifteen years old and later the patient had ophthalmic migraine—*i. e.*, attacks of blindness accompanied by flashes of light—but these had ceased about ten years before he had the oculomotor palsy. The case is evidently one of recurrent oculomotor palsy, and while it does not strictly correspond to Möbius' narrow limitations in the partial palsy, the age of the patient and the preceding attacks of migraine, it does illustrate the symptom-complex as given by Oppenheim. Why, we may ask, should the palsy not be partial even though the cause is an organic one, why should the symptoms not appear at the age of thirty as well as of twenty-five; why should migraine not precede the palsy even for many years? The condition is a symptom-complex not a disease, and the pathology has been determined in only four cases. Indeed, it is questionable whether Ziehen's case with necropsy should be regarded as one of recurrent oculomotor palsy. Is there good reason for excluding such a case as the one reported by Leszynsky?<sup>1</sup>

A woman, aged twenty-nine years, began when six years old to have attacks of headache confined to the right temporal and supra-orbital regions, and invariably accompanied by vomiting. The attacks occurred every five or six weeks. At her twelfth year the headache was associated with ptosis of the right eye, from which she recovered in two weeks, the migraine continuing to occur as before. The second attack of oculomotor palsy occurred in her nineteenth year, with the same kind of pain and vomiting. She had partial ptosis, diplopia, and inability to look upward with the right eye. She improved in three weeks, but the eye did not move upward as well as before for a few months, and then motility was completely regained. The third attack occurred in her twenty-second year, and was characterized by almost complete ptosis, outward deviation of the eyeball, and diplopia. She recovered in about a year. She had five attacks.

It is well to define a symptom-complex sharply, but in the present state of our knowledge regarding recurrent oculomotor palsy,

<sup>1</sup> Journal of Nervous and Mental Disease, 1901, p. 462.

when the ignorance of the pathology is so great, the description may be made too narrow.

One must always remember that a recurrent oculomotor palsy may be the first sign of a general organic disease of the nervous system, like tabes or multiple sclerosis, but in the case we have reported no sign of such disease could be found.

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## MYASTHENIA GRAVIS, WITH PARALYSIS CONFINED TO THE OCULAR MUSCLES.<sup>1</sup>

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OF WILKESBARRE.

MYASTHENIA gravis may present symptoms of implication of the ocular muscles in association with other signs of the disease, but a limitation of the weakness to the ocular muscles is exceedingly uncommon, and cases of this character are not always easy to diagnosticate. W. Sterling<sup>2</sup> has recently reported a case in which the paresis was observed only in a drooping of the upper lids, the ptosis varying in intensity from time to time. The myasthenic reaction was obtained in the biceps, deltoid, and sternocleidomastoid muscles. This was the only case of this character Sterling knew of, but one of us (Spiller), in association with Dr. William Campbell Posey, has observed a similar case, in which bilateral ptosis of varying intensity was the only sign of the disease, except that one other ocular muscle was slightly affected. Dr. Posey will probably report this case. Sterling refers to the cases of Camuset, Karplus, Kunn, and Wilbrand and Sanger, in which the weakness was only in the ocular muscles, although in the first two cases other symptoms of the disease developed later. The myasthenic reaction to the electric current does not seem to have been obtained in any of these four cases.

A case reported by Oppenheim is as follows:

A man, aged forty-seven years, not syphilitic and not alcoholic, in February, 1904, noticed suddenly diplopia. He had some headache during a few days. He was strong, and only the ocular muscles were affected. Both internal recti muscles were paralyzed, and within a few days ptosis, especially on the right side, developed. The intensity of the ptosis varied greatly; at times it was only slightly indicated,

<sup>1</sup> Read before the Philadelphia Neurological Society, January 24, 1905.

<sup>2</sup> *Monatsschrift f. Psychiatrie und Neurologie*, vol. xvi. p. 182. (Erganzungsheft.)

at other times the pupils were almost covered by the upper lids. The levator palpebræ superioris, therefore, appeared to be easily exhausted. If the man were made to look upward, the upper lids began to fall within a few seconds. The action of other muscles (presumably ocular) caused exhaustion of the levator. Occasionally the ptosis was more pronounced on the left side. He had neither diplopia nor ptosis in the morning during an hour after awakening. Myasthenic reaction was observed in the left deltoid. This muscle was not fully exhausted by the electric current, but the contractions became weaker with every irritation. There were no other symptoms of involvement of the nervous system at this time. The right large toe was unusually large. Later bulbar symptoms developed, and the disease terminated fatally.

Oppenheim remarks that these ocular forms of myasthenia gravis have not received sufficient attention, and that probably they are more common than is supposed. The diagnosis of cerebral syphilis or tabes is likely to be made in such cases. Tabetic ptosis may be a hypotonia of the levator palpebræ superioris, and may disappear for a time, and variation in intensity of the ocular palsy is recognized in tabes. The signs of tabes at first may be in the ocular muscles and may be confined to these for a long time. The internal muscles of the eyes are not affected in myasthenia, but these muscles may also escape in tabes. The myasthenic electric reaction is a positive means of diagnosis.

Oppenheim<sup>1</sup> points out that congenital defects have been observed in myasthenia, such as the enlargement of the toe he observed in his case.

The case of myasthenia gravis we report is remarkable, in that the weakness was observed only in the ocular muscles. The rapid exhaustion of the levator palpebræ superioris, first of one side and then of the other, especially when both eyes were uncovered at the same time; the recovery after rest, the variation in the paralysis of other external ocular muscles of the oculomotor distribution, the integrity of the inner muscles of the eyeballs, a response of the sternocleidomastoid muscle to the faradic current, suggesting the myasthenic reaction, and the absence of all other signs of implication of the nervous system, make the case probably one of myasthenia gravis of the ocular type.

*Notes by Dr. Buckman, January 8 and 13, 1905.* C. F. L., aged thirty-three years, a groceryman, muscular, consulted me April 26, 1904, on account of dizziness and blurring of sight, which had lasted about one week. His vision was, and now is, about normal. He complained that everything looked crooked with both eyes, but perfectly normal with either alone. The slight error of refraction

<sup>1</sup> Deutsch. med. Wochenschrift, July 14, 1905, p. 1053; Berliner klin. Wochenschrift, February 6, 1905, p. 164.

was corrected under atropia, and he was ordered for the right eye  $+ .25 \text{ C} + .25 \text{ c. ax. } 90^\circ$ ; for the left eye,  $+ .50 \text{ C} + .25 \text{ c. ax. } 90^\circ$ , combined with prism  $2^\circ$  base up and  $\frac{1}{2}^\circ$  base out. This correction lasted but a short time, and the muscular deviation gradually increased. He could use either eye alone, but could not use both eyes together, and has not been able to do so since that time.

On November 14th there was almost complete paralysis of the inferior rectus muscle of the right eye. The condition improved under large doses of iodide and daily applications of electricity. In a short time from the last date ptosis of the left eye developed, with occasional ptosis of the right. He took mercury to ptyalism and is now taking large doses of strychnine.

Sometimes one muscle is paralyzed and sometimes another. The sixth nerve has never been affected. He has not had optic neuritis, nausea, vomiting, headache, nor vertigo during the past six months. He has not had syphilis, and is not hysterical. His mother and several of his maternal relatives are afflicted with some defect in the ocular muscles.

The headache from which he suffered was purely nasal in origin. He has some hypertrophic rhinitis, and the few headaches he has had since he has been under treatment have been almost immediately relieved by a reduction of the pressure from the enlarged and engorged middle turbinates. The pain has always been unilateral, and it has been entirely absent since his catarrh has been treated regularly.

When he lies flat on his back both lids remain wide open without effort, and all the muscles appear well balanced.

*Notes by Dr. Risley, January 12, 1905.* When first seen by us, October 28, 1904, the following conditions were present: The vision in the right eye, with his correcting glass, was 6/x; in the left eye, 6/viii. The ophthalmoscope showed the fundus oculi cherry-red and fluffy, with large central excavations in the disks, but no signs of atrophy or swelling. There was present diplopia caused by a partial paralysis of the internal rectus, and a complete paralysis of the inferior rectus on the right side. At his next visit, November 25, 1904, the double images were closer together, and a curious ptosis was present, usually affecting the left eye, but at times both eyes. *He stated that on arising in the morning the eyes were wide open, and the double images very close together, and at times he had no perceptible diplopia, but as he resumed the duties of the day all the symptoms recurred.* The left eye at this visit was slightly turned upward, apparently by the effort to overcome the ptosis. There were crossed diplopia and left hyperphoria.

*Examination.* Eyes left=exophoria disappears, hyperphoria increases. Eyes left and up=hyperphoria increases, slight exophoria. Eyes right and up=exophoria increases, hyperphoria disappears. Eyes right=exophoria increases and hyperphoria increases

Eyes right and down=hyperphoria and exophoria increase. Eyes down=exophoria and hyperphoria diminish. Eyes down and left=exophoria and hyperphoria diminish.

Four years ago a friend of the patient, an optician, told him he had muscle trouble when testing his eyes.

*Notes by Dr. Spiller, January 10, 1905.* The patient had severe headache during ten years until about six or seven months ago. Vision was not affected when he had the headache and has always been good.

When he takes off his glasses the upper lids begin almost immediately to droop and continue to do so until the eyeballs are covered, first one then the other. He wears a cover over one eye, and changes this from one glass to the other frequently. When he looks downward both upper lids fall. The external rectus on each side is normal. He cannot look upward or downward very well with the right eye, but can perform these movements with the left eye. He cannot keep both eyes open at the same time more than a minute, but if he covers one eye the other remains open. The iritic response to light and accommodation is prompt in each eye. Sensations for touch and pain are normal in all parts of the body. The muscles of the face, of the tongue, and of mastication are normal. The biceps reflex is not unusually prompt on either side. The grasp of each hand is powerful. Voluntary power in the lower limbs is normal. The patellar reflex is normal on each side. Ankle clonus is not obtained. Gait and station are normal with eyes open or closed. The muscles of the facial distribution respond promptly to the faradic current.

*January 24, 1905.* When he rises in the morning he cannot open his eyes so well as later in the day; formerly this was not the case. He can open his eyes better in the evening; during the entire day he uses his eyes in reading orders in his store (he is a groceryman) or in writing, therefore the disturbance is greater during the day, and is less in the evening, because he lies down.

*When he takes off his glasses the upper lid of one eye, depending on which eye he had been using last, begins to fall, and gradually the upper lid falls until there is complete ptosis; while this is occurring, the upper lid of the other eye gradually droops, until ptosis may be complete or nearly complete on this side.* The falling of the upper lid cannot be due to an attempt to overcome the diplopia, because the second lid droops after the first pupil is covered by the lid, and the falling of the lids occurs in the same manner when occasionally he has no diplopia while looking directly forward. He usually has diplopia in looking directly forward, but occasionally he has no diplopia for a few minutes, and then one eye "shoots off," as he expresses it, and diplopia develops. *When the upper lids have fallen, if he closes his eyes for two or three minutes he can open them again, but with some ptosis of one lid; to-day it is in the left.*

FIG. 1.



The ptosis of the right eye is not so great as that of the left. The photograph was taken one or two minutes after the glasses were removed. At times he is able to open both eyes fully.

FIG. 2.



The eyeballs are almost completely covered. The photograph was taken after the glasses had been removed three or four minutes.

He cannot keep both eyes open at the same time more than one or two minutes. If he covers the left eye with his hand, the right eye stays open better, but after two or three minutes the right upper lid falls. He now can keep the left eye partially open if he covers the right eye. The weakness of the other ocular muscles seems now to be in the elevators and depressors of the right eyeball. The ocular palsy, he says, has seldom been the same at any two examinations. The deltoids react well to a rapidly interrupted faradic current, but there seems to be some exhaustion by this current in the left sternocleidomastoid muscle.

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## MYASTHENIA GRAVIS:

WITH SPECIAL REFERENCE TO THE OCULAR SYMPTOMS, AND A REPORT OF A CASE INVOLVING THE EYES ONLY.<sup>1</sup>

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MYASTHENIA gravis is rare, especially in children. Of the earlier investigators, six are pre-eminent, viz., Wilks, Erb, Oppenheim, Hoppe, Goldflam, and Jolly. The disease was first described by Wilks<sup>2</sup> in 1877. He recorded a case of apparent bulbar paralysis, in which death resulted in a few weeks from failure of respiration. No lesion of the medulla was found at the autopsy. In 1878 Erb<sup>3</sup> published three cases, in two of which the principal symptoms were bilateral ptosis, while in the third, the intrinsic muscles of the eye were also involved. Weakness of the neck muscles, paresis of the muscles of mastication and weakness of the tongue and extremities were other symptoms observed. No muscular atrophy was present. Nothing more was added to the subject until nearly ten years later, when Oppenheim,<sup>4</sup> in 1887, published "A Case of Chronic Progressive Bulbar Paralysis without Anatomical Findings." Shortly afterward Eisenlohr<sup>5</sup> reported a case in an eighteen-year-old girl, in which the prominent symptoms were ptosis and paresis of other ocular muscles. In this case, as in Oppenheim's, no lesion was found. In 1891, Goldflam<sup>6</sup> added four new cases to those previously reported and collected by him. In 1892 Hoppe<sup>7</sup> contributed an exhaustive account of the subject, signaling a new epoch in the history of the disease. Goldflam showed that the characteristic

<sup>1</sup> Read before the Chicago Medical Society, November 2, 1904.

<sup>2</sup> Guy's Hospital Reports, 1877, vol. xxii.

<sup>3</sup> Ueber Einen Neuen, wahrscheinlich bulbären Symptomenkomplex, Arch. f. Psych., Bd. ix.

<sup>4</sup> Virchow's Archiv, Bd. cviii.

<sup>5</sup> Neurol. Centralbl., 1887, Bd. vi.

<sup>6</sup> Ibid., 1891, Bd. x.

<sup>7</sup> Berl. klin. Woch., 1892, Bd. xxix.

muscular symptoms—fluctuating in intensity, improving by rest and becoming aggravated by fatigue and exertion—were an abnormal tiring rather than an absolute paresis. As an addition to the clinical picture Jolly,<sup>1</sup> in 1895, described the peculiar electric reaction of the nerves and muscles known as the “myasthenic reaction”—*i. e.*, the muscles and nerves reacting normally to electricity are rapidly exhausted by the faradic current, but respond again after rest. This electric reaction is quite variable. In some cases it is marked, in others slight. It may be present at one time, and absent at another in the same case. Again, it is often present in a certain group only of the affected muscles. The number of names by which the disease is known is numerous. Among them are bulbar paralysis without anatomical lesions, *maladie d’Erb*, *syndrome d’Erb et Goldflam*, *myasthenie grave pseudoparalytique* (Jolly), chronic progressive bulbar paralysis (Oppenheim). Strümpell<sup>2</sup> called the affection asthenic bulbar paralysis.

The most salient features of the disease are briefly as follows:

**ETIOLOGY.** Sex has a marked influence. The disease is most frequent in the female. Of the reported cases, there were nearly twice as many females as males. It appears most often between the ages of twenty and thirty years. Only three cases under ten years of age have been reported. One of these was a child of four years (Karplus<sup>3</sup>), and another of five years (Goldflam).<sup>4</sup> A third was a child of eight years (Gowers).<sup>5</sup>

No real cause for myasthenia gravis is known. Some prostrating infectious disease, such as tuberculosis, influenza, typhoid, diphtheria, etc., frequently precedes the affection. Toxic causes, as alcohol, rheumatism, and syphilis, have been assigned, but their significance is unknown. Anæmia, menstrual disorders, and pregnancy were noted in women. Mental strain and anxiety, exertion and migraine, occasionally precede myasthenia gravis.

**ONSET.** This is usually gradual; but occasionally the symptoms increase quite rapidly, death resulting within a few weeks. Such a case is reported by Devendorf.<sup>6</sup> Weeks, months, or years elapse sometimes before symptoms of the disease appear other than ocular paresis. In Karplus’<sup>7</sup> patient ocular paralysis occurred at intervals for nineteen years before any other signs of the disease were observed.

**SYMPTOMATOLOGY.** An early and most important symptom coming on gradually and insidiously is ptosis. In nearly half the cases this was the first symptom to appear. It was present in over 80 per cent. of all recorded cases. “When it is remembered how easy it is for a patient to overlook a slight ptosis, this proportion

<sup>1</sup> Berl. klin. Woch., 1895, Bd. xxxii.

<sup>2</sup> Deutsch. Zeitschr. f. Nervenheilk., 1896, Bd. viii.

<sup>3</sup> Jahrb. f. Psych. u. Neurol., 1897, Bd. xv.

<sup>4</sup> British Medical Journal, 1902, vol. lxxxv.

<sup>5</sup> Deutsch. med. Woch., 1902, Bd. xxviii.

<sup>6</sup> Neurol. Centralbl., 1902, Bd. xxi.

<sup>7</sup> Ibid.



FIG. 1.



Position of the lids when no effort is made to raise them. Note the inability to completely close the lids.

FIG. 2.



Strong effort made to raise the lids. The absence of wrinkles in forehead is very noticeable.

seems all the more remarkable" (Hun).<sup>1</sup> As a rule, the ptosis is unilateral at the onset, but it soon becomes bilateral and more marked on one side than on the other, as in the case reported (Figs. 1 and 2). In the morning after the night's sleep it may not be present, but shortly after the patient rises it rapidly becomes marked, and is always worse toward the end of the day or after looking up for any length of time, when the lids gradually droop. Compensatory action from the occipitofrontalis muscle, present in other forms of ptosis, is wanting, due to its own weakness (Fig. 3). Owing to the ptosis and the weakness of the occipitofrontalis muscle the head is thrown back to enable the patient to see. The

FIG. 3.



Eyes were bandaged for ten seconds. The difference between the two eyes is well marked.

double ptosis and the effort made to see causes a sleepy appearance. Unilateral ptosis is reported by Goldflam,<sup>2</sup> Fajersztajn,<sup>3</sup> Kowjewnikoff,<sup>4</sup> and Raymond.<sup>5</sup> Complete and persistent ophthalmoplegia externa occurs without exception at some period of the disease. Although the ocular paralysis affects the extrinsic muscles of the eye, the intrinsic muscles are never paralyzed. Reaction of the pupils to light and accommodation always seems to be normal. In a doubtful case reported by Brissaud and Lautzenberg<sup>6</sup> the

<sup>1</sup> Albany Medical Annals, January, 1901.

<sup>2</sup> Deutsch. Zeitschr. f. Nervenheilk., 1893, Bd. iv.

<sup>3</sup> Neurol. Centralbl., 1896, Bd. xv.

<sup>4</sup> Deutsch. Zeitschr. f. Nervenheilk., 1897, Bd. ix.

<sup>5</sup> Gaz. des hôpitaux, 1900, tome xxi.

<sup>6</sup> Arch. gén. de méd., Mars, 1897.

light and accommodation reflexes of the pupil were abolished. Inequality of the pupils has been noted, and in a case reported by Buzzard<sup>1</sup> the pupils showed a tendency to oscillatory movements after prolonged convergence. There is frequently an inability to completely and firmly close the lids. This is present in the case herewith reported (Fig. 1). Owing to the weakness of the orbital muscles, diplopia is often present. This is associated rarely with irregular nystagmoid movements, produced by lateral conjugate deviation of the eyes. Strabismus is often present (Fig. 4). A slight prominence of the globe has been observed in a number of

FIG. 4.



Showing the divergence of the right eye.

cases, probably due to the weakness of the recti and the orbicularis palpebrarum muscles. Exophthalmos with symptoms of Basedow's disease was present in cases reported by Jendrassik,<sup>2</sup> Goldflam,<sup>3</sup> Karplus,<sup>4</sup> Oppenheim,<sup>5</sup> and others. The muscles of mastication are very commonly implicated, so that eating is a slow and difficult process from their rapid exhaustion. The muscles of deglutition are often involved, so that food collects in the roof of the mouth and is swallowed with difficulty, and liquids regurgitate through the nose, owing to the weakness of the palate. Choking while

<sup>1</sup> Transactions of the Ophthalmological Society of the United Kingdom, vol. ix.

<sup>2</sup> Arch. f. Psych., 1886, Bd. xvii.

<sup>3</sup> Ibid.

<sup>4</sup> Ibid.

<sup>5</sup> Monograph, Die Myasthenische Paralyse, Berlin, 1901.

eating is very likely to occur, on account of the diminution in the pharyngeal reflex. Weakness of the pharyngeal muscles is uncommon, but has been observed with the laryngoscope in the cases of Hoppe,<sup>1</sup> Buzzard,<sup>2</sup> and Oppenheim.<sup>3</sup> The speech, at first normal, shortly becomes nasal and the words grow more and more indistinct, until there is complete aphonia. Neither muscular atrophy nor the reaction of degeneration is ever present. Pain is a rare symptom. The muscular symptoms are, as a rule, bilateral. The weakness of the muscles results in their rapid exhaustion upon active movements. Bulbar paralysis is present to a greater or less degree, and finally dyspnoea after exertion is a striking symptom. From this the patients usually die. The phenomenon of muscle tiring and permanent paresis is found in those voluntary muscles which are continually in tonic contraction and have little rest, such as the levator palpebræ, the muscles of expression and mastication. The purely reflex acts of the eye and extremities do not show any abnormal tiring, Jolly,<sup>4</sup> Buzzard,<sup>5</sup> Campbell,<sup>6</sup> and others. This phenomenon of weakness, as a rule, is not present in all of the muscles, but is limited to a few muscles or a group of muscles, as in the case reported. This particular symptom may wholly and unexpectedly remit for several days. Indeed, remissions and exacerbations are the rule, but the weakness is always worse in the evening.

**PATHOLOGY.** The pathology is vague and uncertain. In the autopsies that have been made there is no evidence that the disease is associated with any lesion of the nervous system. In over half the cases no lesion was demonstrable. Many hypotheses have been brought forward in explanation of the symptoms, but as to the exact nature of the disease we are profoundly ignorant. From the clinical conditions, gross lesions could not be expected.

**PROGNOSIS.** Judging from the reported cases, the prognosis as regards recovery is practically hopeless. Apparent recovery has been noted, but when we recall the great improvement and apparent recovery lasting weeks, months, or years, and followed by a relapse we must look upon permanent recovery as doubtful. The average duration of the disease is from one to three years. Of the one hundred and twenty cases referred to fifty died.

**DIAGNOSIS.** The diagnosis is easy in typical cases when the rapid tiring and variation in the intensity of the symptoms with the myasthenic reaction appears; but the diagnosis is especially difficult, and at times impossible, in the early stages of slowly developing and atypical cases. The possibility of hysteria being mistaken for this disease is great, especially when the only symptoms are ptosis

<sup>1</sup> Monograph, Die Myasthenische Paralyse, Berlin, 1901.

<sup>2</sup> Ibid.

<sup>3</sup> Ibid.

<sup>4</sup> British Medical Journal, 1899, vol. i.

<sup>5</sup> Ibid.

<sup>6</sup> Ibid.

and diplopia, appearing and disappearing without apparent cause. Ocular paralyses, rapid tiring of the muscles are rarely found in hysteria, while the myasthenic reaction is not. As in other hysterical paralyses, those of the eyes are characterized by their lack of permanency, their change under psychic influences and their association with sensory disturbances and other hysterical stigmata. In the early stages of the disease it might readily be mistaken for nuclear ophthalmoplegia, and when the ophthalmoplegia alone is present, the diagnosis is extremely difficult. In myasthenia gravis the muscles regain a certain amount of power after rest, but sooner or later the other symptoms of the disease appear. In pseudo-bulbar paralysis the ocular muscles are not involved, and the myasthenic reaction and rapid tiring are not present.

**TREATMENT.** The treatment consists first in absolute rest, gentle massage, and measures to maintain a high standard of nutrition. A mild galvanic current has been used, but its benefits are questionable. Many drugs have been tried, but none seems to have any favorable influence over the progress of the disease. The case about to be described illustrates very nicely the ocular phase of the disorder.

The patient, E. M., a female, aged ten years, of American birth, but of Bohemian parentage, was referred to me in November, 1902. At the time of my first examination there was present double ptosis, most marked on the right side (Figs. 1 and 3), paresis of all the extrinsic muscles of both eyes, and a marked divergent squint of the right eye (Fig. 4), with complete preservation of the functions of the intrinsic muscles. The iris reacted to both light and accommodation. The fundi were normal, and save for an error of refraction—O.D. +1.50—3.50 X 180° V. 6/9+: O.S.—1.25 X 180° V. 6/5—the visual faculty was normal. Her history is as follows:

In 1898, when the patient was four years old, she was ill, but nothing further can be learned. Two years following, in 1900, her mother first noticed a drooping of the right eyelid, and a few weeks later the left became affected. She was taken to the Illinois Charitable Eye and Ear Infirmary in November, 1901, and all that the records there show is the following:

“Case No. 108,110, E. M.; mixed astigmatism; ptosis acquired one year; defective motion of all external eye muscles except left external rectus.” The child is well nourished, and repeated examinations show nothing abnormal with any other functions of the body. From the beginning there was no evidence of ptosis upon getting up in the morning, but gradually the drooping becomes marked as the patient gets about. Early in the history the ptosis disappeared entirely for a day or two, only to return again. The eyelids can be closed, but not tightly, and, owing to the weakness of the occipitofrontalis, the forehead can be moved but very little. The patient tries to overcome the ptosis by throwing her head back.

With the persistence of the ptosis there was observed a gradual progressive impairment of power in the movements of the eyeballs, but without diplopia. This increased until the eyes became completely fixed in the primary position. At the present time there is about one millimetre of lateral excursion in either eye, but motion is barely perceptible in the vertical. If the eyes are bound lightly with a bandage or even kept closed for a few seconds, the movement of the lids appears normal (Fig. 2), but raising the lids three or four times in succession causes complete exhaustion. The movement of the globes improves only slightly with rest. A feeble myasthenic reaction has been demonstrated at times, and when sought for again was entirely absent. There is no history of tuberculosis, syphilis, or nervous disease in the family. There is nothing abnormal in the motor or sensory distribution of the fifth nerve.

Let us now consider what the nature and seat of a lesion would probably be that would cause an impairment of function of part of the third nerve and also the fourth and sixth on the same side, and do no damage to the structures in the immediate vicinity. An intraorbital lesion of the third nerve, or one involving its intracranial trunk, would not account for it, for the ciliaris or the sphincter iridis would not escape. Could a gross lesion, such as a tumor, meningitis or an area of softening, affect the nuclei of the third, fourth, and sixth nerves, and at the same time not involve the centres for the iris and ciliary muscle, the fifth and seventh or other neutral tracts? To this question we must answer no, excepting that we assume several independent lesions have involved the nuclei of a set of associated nerves on both sides, which is quite improbable. The most rational hypothesis, then, is that the disease is purely a motor one, and that the lesion must be situated either in the muscles themselves or in the motor nuclei. It has been demonstrated by Hensen and others that the innervation of the sphincter of the iris and the ciliary muscles arises from nuclei separate and distinct from those giving origin to the remaining parts of the third nerve. The myasthenic reaction, and the nature and distribution of the symptoms, point to a disturbance in the muscles or the peripheral motor neurons, rather than to a lesion in the motor nuclei. Whether this can be explained as due to the action of a toxin powerful enough to produce symptoms of the disease, and yet produce no demonstrable structural changes, or to lymphoid infiltration of the muscles as found by Weigert,<sup>1</sup> Goldflam,<sup>2</sup> Link,<sup>3</sup> and Hun,<sup>4</sup> is a question unsettled, as yet. Until some definite and characteristic anatomical lesions are proven, we can only theorize.

<sup>1</sup> Neurol. Centralbl., 1901, Bd. xx.

<sup>3</sup> Deutsch. Zeitschr. f. Nervenheilk., 1902, Bd. xxiii.

<sup>2</sup> Ibid.

<sup>4</sup> Ibid.

## MYXŒDEMA FOLLOWING EXOPHTHALMIC GOITRE.

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FROM time to time there have been reported cases of myxœdema which either preceded or followed upon exophthalmic goitre. The following case is one in which, to use the terms of Moebius and Greenfield, athyrea succeeded upon hyperthyrea. The notable feature of this case is the remarkable amount of gastric disturbance that the patient has suffered, and, to a less extent, still experiences; otherwise there can be claimed nothing peculiar; similar cases have been reported by Kraft-Ebing, Felin, Fauer, and Osler.

Rebecca L., aged fifty-seven years, married, housewife, was admitted to the New York Hospital December 11, 1903; service of Dr. Peabody. The patient complained of nervousness and weakness.

*Family History.* There is no history of tuberculosis or cancer. None of her relatives has had joint diseases. Her parents, brothers, and sisters are free of any nervous troubles, and she knows of no one in her family that ever had a goitre.

*Past History.* She does not remember any disease in childhood. She had typhoid fever "many years ago," but has never had chills and fever, pneumonia, nor pleurisy. She has had various rheumatic "twinges," but has never been sick in bed with joint pains. She has never been jaundiced. There is no history of chronic cough or of any symptoms of pulmonary disease. The patient states that she has not suffered from shortness of breath in past years, and her ankles have never been swollen; her appetite has been moderate, food never causing distress; bowels usually regular.

The menses have been regular, but always attended with some pain. She has been married a number of years (cannot recall the year of marriage), but has never had a child. There have been no miscarriages. The patient was operated upon at the Roosevelt Hospital in 1901 for uterine fibroids, the uterus being removed, but not the ovaries.

*Present Illness.* The patient affirms that aside from always being very nervous, she has enjoyed good health until the onset of the present affection. In 1887, after returning from South America, she noticed that her neck was considerably swollen. This increase in size continued for some time; she is not sure how long. She was then told that she had a goitre. At this time the patient says she was "horribly" nervous, her hands shaking violently, and she suffered from palpitation of the heart. Her friends often told her that her eyes were "swollen." She thinks that she continued in this

condition without much if any change until six months previous to entering the hospital. Over a year ago, however, she says that she noticed that her skin was very dry and came off in fine scales, and that her hair was dry and becoming thin rapidly. A leukodermic spot on her hand was much more marked then than at present.

About six months ago the patient says the palpitation of the heart became considerably aggravated, and that she had dull, aching pains in her legs. At about this same time her body began to swell, and she became "puffy" all over. Her strength was so lacking that she could not leave her bed, and there she remained for seventeen weeks. During this time she was utterly wretched from the nervousness and the aggressive sense of weakness, and frequently meditated on self-destruction. Her memory was very defective then, she thinks, and is now, since she recalls events slowly and with evident effort. While in bed she vomited frequently, lost her appetite, and ate only when urged to do so. She says she vomited several times every day, and that some degree of nausea was constant. The vomiting had no relation to the taking of food, the vomited material consisting usually of clear mucus, which had an extremely offensive odor. The patient states that this was so disgusting a feature that it was necessary to place her in a room remote from others in the family. The vomitus was always large in amount, on one occasion being so much during the course of the day that the attending physician measured it, and told her it was nine pints. This symptom gradually abated, but she gained no strength. During this seventeen weeks in bed she had no pain, her suffering being purely nervousness, an oppressive sense of impending misfortune, and complete prostration from weakness.

Her general condition improved, however, and, as her physician gave her no hope of further help, she came to the Out-patient Department of the New York Hospital, where she was treated with thyroid extract during the two weeks previous to admission to the wards. There appear no illusions or mental defects in the patient at present, other than slowness of cerebration and defective memory mentioned above.

*Physical Examination.* The patient has rather a bloated appearance, and the flesh is soft and flabby. She does not look anæmic. Her hair is quite thin and feels dry and harsh. The skin is dry, and on the body a fine, branny dust can be removed. The eyes appear normal. There is a slight tremor in the muscles of the face, and some pulsation of the veins of the neck. The thyroid gland cannot be felt. The heart is normal.

Pulse is regular, 100 to the minute, good size, moderate force and tension; the artery wall is not thickened. The lungs and abdominal organs present nothing abnormal.

*Extremities.* There is slight œdema of the feet; the knee-jerks are exaggerated; there is marked tenderness to pressure over the



course of both sciatic nerves. The axillary and inguinal glands are not palpable. The urine and blood are normal.

The patient was given 5 grains of thyroid extract daily, in addition to a general tonic treatment of stomachics, cold packs at night, etc. Her improvement was not marked at the end of two weeks, and the thyroid extract was doubled in dose, which caused some diminution of the nervous symptoms. A dose of 15 grains of thyroid daily was tried, but caused a marked increase in the patient's irritability and cardiac palpitation, on account of which the 10-grain dose was resumed. Improvement was very slow, but the patient was able to leave the hospital after two months (February, 1904) much less nervous and decidedly altered in appearance, the bloated, stupid look in the face having quite disappeared. She was, however, far from well, being mentally depressed and without energy.

*June 15, 1904.* There is no evident change in the patient's condition; she is still nervous, weak, and mentally depressed. She does some of the household duties, but says they quite exhaust her. She is still taking 10 grains of thyroid extract daily. Her general nutrition is good; hæmoglobin, 90 per cent.; urine, normal.

*September 20th.* Since last seen the patient has suffered several attacks of diarrhœa. She says she has pains in her abdomen every few days. When these pains are quite severe it marks the commencement of a diarrhœal attack. Her general condition, nutrition, and mental tone are not changed.

Physical examination is quite negative. She now has the harassed look of an individual suffering from one of the milder forms of insanity, and she says she is constantly worried, though she knows no cause for anxiety. Her sleep is disturbed, and nights pass when she does not sleep at all. An endeavor has been made to regulate these nervous phenomena by means of tonics and sedatives, but with no apparent success.

What may be the state of the gastric secretion, we can only conjecture, as attempts to recover a test-meal have been futile; the stomach tube causes so much distress to the patient that the experiment has been abandoned.

It appears at present that this patient is as well as she ever will be, and that she is doomed to drag out a wretched existence, unless some kindly acute infection releases her.

These cases of myxœdema following exophthalmic goitre are rare enough always to excite our interest. It is evident from cases like the above that in this type of myxœdema there is another element besides deficiency of thyroid function, or else the administration of the gland extract would produce better results. It may some time be shown that there is a perverted function as well.

## THE RESULT OF SPLENIC REMOVAL:

WITH THE REPORT OF THE SUCCESSFUL REMOVAL OF A WANDERING  
SPLEEN WITH A TWISTED PEDICLE, OCCUPYING THE LEFT  
ILIAC REGION, WITH PERISPLENITIS AND  
NECROSIS OF THE PULP.

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THE spleen, like the stomach, has generally been considered a vital spot of the human economy. It was formerly taught that the loss of either meant instant death. But during the last few years we have seen the removal of both, and we are led to believe that neither is essential. The digestive function can be entirely assumed by the intestine, and, though a frequency of eating be demanded, there is no impairment of health. Whatever the function of the spleen, whatever the compensatory changes when removed, we are beginning to realize that in many cases a splenectomy is not only justifiable, but eminently to be sought. It is in this connection that I wish to report a case of wandering spleen with twisted pedicle, occupying the left iliac region, a perisplenitis, and a necrosis of the pulp.

On account of the close anatomical relation which the spleen bears to the stomach, it was but natural to suppose that in some way the organ was concerned in digestion or metabolism. Along this line there have been many investigators. No suitable explanation has, however, been offered for the splenic enlargement occurring in most of the acute infectious diseases. Whether the spleen plays any role in the production of toxins or antitoxins is not known. Yet, Courmont and Duffon<sup>1</sup> found that spleenless animals resist diphtheria better than normal ones, and the more recent the removal the more marked the resistance.

Noël Patton,<sup>2</sup> after an extensive series of experiments upon the spleenless dog, concludes (1) "that there is a more rapid excretion of water after a meal, probably indicating a more rapid absorption," and (2) "that there is no essential difference in the course or nature of the metabolism either during fasting or after feeding with the ordinary proteids of flesh, with vegetable food such as oat-meal, or with food rich in nucleins such as thymus gland." The later work of Fourin<sup>3</sup> confirms this. He removed both the spleen and stomach, and finds that, while there may be a temporary derange-

<sup>1</sup> *Archiv. de méd. expér. et d'anat. path.*, Mai, 1898.

<sup>2</sup> *Journal of Physiology*, 1900, vol. xxv. p. 442.

<sup>3</sup> *Comp.-ren. des séances et mém. de la Soc. de biol.*, 1902, tome iv. p. 418.

ment of the digestion due to the removal of both spleen and stomach there is no permanent interference.

The formation of uric acid has been ascribed to the spleen. Lo Monaco,<sup>1</sup> however, found that the output of uric acid in a spleenless patient fed on a mixed diet was approximately normal; and in no case was it noticeably diminished. Similarly, the work of Mendel and Jackson.<sup>2</sup> To quote: "Our experiments demonstrate that the spleen is by no means the chief organ involved in uric acid production, if, indeed, it normally plays any part whatever in the process. It seems improbable, therefore, that the formation of uric acid in the mammalia can be assigned at present to any definite organ or group of organs." My own case illustrates this also. Though no special examinations were made of the patient's urine, there was no reason for suspecting the slightest abnormality.

What then is the splenic function? Let us turn to its histological structure. Without going into details, we shall remember that it is composed of a reticular network filled in with both red and white blood corpuscles, as well as some large amoeboid cells (the so-called spleen cells), and that surrounding the terminal arterioles there are masses of true lymphoid tissue (the Malpighian bodies). Bland Sutton<sup>3</sup> remarks that the spleen is to be "regarded as a highly developed and specialized lymph gland." If one kidney be removed the other will assume the work of both and may or may not hypertrophy. So it appears that if the spleen is removed the lymphatic glands perform its duties. There is no constitutional disturbance, and the only clinical data to be observed is a change in the structure of the blood. Thus it is proved that the splenic function deals with the blood, but just how is as yet unanswered. Many have supposed that the spleen is in some way a numerical regulator of the corpuscles, and perhaps destroys the broken-down erythrocytes. But this, with our present knowledge, can neither be affirmed nor denied.

The work of Vincent<sup>4</sup> is conflicting. Examining the anatomical changes in the spleenless dog, he finds in one (that furnished him by Professor Shafer, fifteen months after operation) no increase in either the size or number of the ordinary lymphatic glands, but an increase in the hæmolymph glands, "the amount of hæmolymphatic structure being decidedly greater in this spleenless dog than under normal circumstances." But no such change was noticed in five other spleenless dogs. Indeed, to quote his own words, "there was no apparent change in the lymphatic glands of any part of the body, neither in the direction of hypertrophy nor increased redness. On microscopic examination the hæmal lymphatic glands presented the features of those in a normal dog. The

<sup>1</sup> Bull. della Soc. Larcisiani degli Ospedali di Roma, 1894, vol. xiv. p. 102.

<sup>2</sup> American Journal of Physiology, 1900, pt. iv. p. 163.

<sup>3</sup> Lancet, January 16, 1897, p. 174.

<sup>4</sup> Journal of Physiology, 1900, vol. xxv. p. 2.

red bone-marrow appeared to have its usual structure." He could not say whether this was increased or not.

The work of Warthin<sup>1</sup> upon the sheep seems to agree with Vincent's first results. He describes a "hyperplasia of existing lymphoid tissue, transformation of hæmolymp nodes into ordinary lymphatic glands, and a new formation of hæmolymp nodes out of lobules of fat tissue, and a later proliferation of the red marrow." He finds no evidence of the formation of red blood cells in the lymph nodes after splenectomy. "The function of hæmolysis is taken up first by the hæmolymp nodes, later by the ordinary lymphatic glands." Continuing, he remarks that "the hæmolytic function of the hæmolymp nodes and hyperplastic lymph glands exceeds that of the primitive spleen, causing an excessive destruction of red cells. The resulting anæmia is later compensated for by an increased activity on the part of the bone-marrow. It would appear, therefore, that the removal of the spleen leads to an increased production or retention of some hæmolytic agent usually disposed of by the spleen. The effect of this hæmolytic agent is either to stimulate the phagocytes in the hæmolymp nodes to increased activity, or to change the red cells so that they are more easily destroyed by these phagocytes." "The presence," he concludes, "of great numbers of eosinophiles in the glands, showing great destruction of red cells, seems to point to some relationship between these cells and hæmolysis." He confirms the appearances described by Tizzoni, Wimgradow, Eterod, Griffin, and Mosler, but interprets them differently. He also confirms Bayer's work upon the regeneration of the lymph glands.

Thus it is conclusively proved that the lymphatic glands take up the work of the spleen. These may or may not enlarge or undergo a change; different species seem to react differently, or even individuals of the same species. In human beings the result is still doubtful, although Mendel and Jackson state that an enlargement of the lymphatic glands has been recorded after splenectomy. Bayer<sup>2</sup> declares that enlargement of the thyroid and lymphatics occurs in many cases, though transitory. But I would mention that a most careful examination of the cervical glands, thyroids, and tonsils of my own patient showed no abnormality. What compensatory changes occurred in the mesenteric glands, I am, of course, unable to say.

According to Bayer, the immediate results of splenectomy are an increase of the leukocytes, a decrease of the erythrocytes, and a reduction of the hæmoglobin. These and the changes noted above are only transitory; in the course of a week or month the blood will become normal. Cabot<sup>3</sup> states that after splenectomy from

<sup>1</sup> Contributions to Medical Research, Ann Arbor, 1903, p. 234.

<sup>2</sup> Münchener medizinische Wochenschrift, Bd. li. p. 116.

<sup>3</sup> Clinical Examination of the Blood, New York, 1904, p. 181.

whatever cause there is a lymphocytosis. "Later, after many months, a moderate eosinophilia may appear and the mast cells are increased." In 3 cases cited by him the white blood count ranged from 17,500 to 27,000 in from five weeks to two months after operation. In 21 cases collected by Stahelin<sup>1</sup> there was a leukocytosis varying from 12,000 to 60,000 per cubic mm., according to the length of time, usually from 10,000 to 17,000.

Rautenberg,<sup>2</sup> so far as I can observe, has published the best set of observations. His case showed immediately before operation some 5000 white blood cells. Three days afterward it had risen to 6500, and gradually increased until the thirtieth day, when a maximum of 10,000 was attained. There was then a gradual fall, until nine and a quarter months after operation, when it reached 5300, only to rise later to 6500. The reds rose from 4,310,000 to 5,100,000, attaining a maximum at the same time as the whites, and falling within ten months to 3,750,000. In the meanwhile the lymphocytes had increased from 19.3 per cent. to 33.4 per cent., when they, too, began to fall; the eosinophiles reached 8.8 per cent. All these changes, except the last one, occurred when the leukocyte count was the largest, some thirty days after operation.

Stahelin's case, like my own, was complicated by an abscess. His counts, made from two months to fourteen months after operation, showed changes similar to Rautenberg's, the blood finally becoming almost normal. Below will be found some comparative counts.

	Reds.	Hæmo- globin.	Whites.	Polymor- phonu- clears.	Lympho- cytes.	Large mononu- clears.	Baso- philes.	Eosino- philes.
Rautenberg:								
Before operat'n	4,310,000	...	5,000	75.6	19.3	1.6	1.3	2.2
30 days after	5,100,000	...	10,000	62.0	31.8	0.4	0.8	5.4
9¼ months	3,720,000	...	5,300	61.2	28.4	1.2	2.0	7.2
Stahelin:								
2 months after	4,700,000	...	15,700	34.2	59.1	2.2	0.3	4.2
6½ months	3,500,000	...	10,000	67.9	26.7	1.8	0.1	3.5
14 months	5,300,000	...	7,500	58.5	35.9	1.75	0.15	3.7
Webster: <sup>3</sup>								
6 days	4,300,000	60	22,000	77.0	14.0	8.0	0.0	2.0
26 days	4,420,000	...	11,600	65.2	12.0	18.8	0.0	2.0
My own case:								
6 weeks after	5,000,000	95	14,400	43.0	42.3	10.7	1.5	2.5

The fever after a splenectomy runs no special course. It is only necessary to remember that in the weakened state of the body any latent or intercurrent disease (such as malaria) will develop. Rou-

<sup>1</sup> *Deut. Archiv f. klin. Med.*, 1903, p. 364.

<sup>2</sup> *Münchener medizinische Wochenschrift*, 1903, No. 16, p. 684.

<sup>3</sup> *Journal of the American Medical Association*, 1903, vol. xl. p. 887.

tier,<sup>1</sup> of Paris, reports the removal of a spleen weighing 3080 grams (six and three-fifths pounds). There was no histological abnormality, but, as the patient had a chill followed by a temperature of 40° C. (104° F.) every five days, he concluded that he was dealing with a malarial (paludique: "salt water") enlargement. I have been unable to refer to Moraczewski's paper<sup>2</sup> on the course of fever after a splenectomy, but would say that in my own case I could find nothing not better explained upon other grounds. The development of an intermuscular abscess caused a rise of temperature as high as 104.4° F. (40.2° C.) on the fifth day, which gradually subsided after a thorough drainage. A secondary rise of temperature yielded to quinine, and I would conclude, like Routier, that a latent malaria was present, especially as the patient was from a malarial region. Aside from this nothing abnormal was noted.

The statistics of splenectomy show a constant improvement. Thus, to quote Bayer: "Bessel-Hagen reports up to the year 1900 a total of 358 cases of total extirpation of the spleen, which does not include those spleens projecting through a peritoneal wound (according to Jordon 28 in all), and which were removed with cure. Of the 358 cases of Bessel-Hagen there were 225 cures and 133 deaths. The mortality is then 37.2 per cent., whereas in the six earlier years it was, according to Vulpius, 49.6 per cent., and according to Ceci, 51.6 per cent. The difference in these statistics, resulting in only six years, shows a great improvement. But Bessel-Hagen says that if those cases were omitted which to-day would be considered inoperable, the percentage of deaths would be reduced, namely, 27.6 per cent. deaths. He goes farther and compares those cases which were operated upon up to the year 1890 with those until 1900. Whereas it was at first 42.2 per cent., it was for the years 1891 to 1900 only 18.9 per cent. Moreover, it is interesting to note that Bessel-Hagen does not consider 10 cases of malarial hypertrophy, which befel one surgeon (Jonesco) and which were moribund, as well as a case of idiopathic hypertrophy whose disastrous result was due wholly to a mistake of the operator, as unavoidable. But if we consider the admission of these 11 cases as arbitrary and therefore inadmissible, there is a reduction of the mortality from 42.2 per cent. during the time up to 1890 to 26.3 per cent., including the years from 1891 to 1900."

Osler,<sup>3</sup> on the other hand, in the 1902 edition of his work, reports (on the authority of Warren) a total of 43 splenectomies for myelogenous leukæmia, of which only 5 recovered. "Fussell," he says in the 1900 edition, "gives the statistics of 105 cases of splenectomy with 48 deaths. Of the cases of simple hypertrophy, 28 in number, 9 recovered. Of 16 cases of floating spleen, 15 recovered." Bayer

<sup>1</sup> Bull. et mém. de la Soc. de chir. de Paris, 1904, p. 366.

<sup>2</sup> Gaz. lek. Warszawa, 1902, q.-s. xxii. p. 868.

<sup>3</sup> Principles and Practice of Medicine, New York, 1900 and 1902.

himself gives a series of 27 wandering spleens with only 2 deaths, while Bland Sutton succeeded in collecting a score of cases operated on within the years 1877 to 1897 without a death. Thus it would seem that, with properly selected cases, the recoveries after splenectomy should equal those of any other abdominal operation.

On August 30, 1904, Mrs. E. consulted me, complaining of a tumor in the left iliac region. She had noticed a small tumor some seven years ago, frequently changing its position, but as it gave no trouble no particular attention was paid to it. It had, however, gradually enlarged. About four months prior to her visit she had strained herself while picking strawberries, and had had frequent attacks of pain in the region of the tumor, which meanwhile had assumed a rapid growth. An examination showed an elliptical tumor in the left iliac region, some soreness, and a slight fluctuation. A later vaginal examination gave no additional evidence. The patient then stated that the tumor had at one time occupied the right iliac region, and that in her youth she had had a "spleen," which, however, disappeared after treatment. Whether this had anything to do with the later developments I cannot say, but it does not seem improbable.

Her family physician, Dr. J. M. Newbern, writes that Mrs. E. was married at sixteen, and has had five children (the youngest three), but no miscarriages. Her health had been fairly good until some nine months before her recent attack, on June 24th, though previous to her marriage she had suffered with malaria and chlorosis. Enjoying a good appetite, she would sometimes eat too heartily, with a resulting attack of indigestion; no pain in the abdomen, but a severe one just under the left scapula. "I called to see her on June 24th," continues Dr. Newbern, "and found her with a high fever, intense pain in the left iliac region, and also a hard tumor. It was so painful that I could not examine her carefully. Her bowels were constipated, and it was with much difficulty that I got them opened."

At the time of the operation it was noticed that the tumor had moved nearer the midline, but I judged that its altered position was due to the emptying of the bowel. Upon opening the abdomen, I found a large brown mass of a semisolid consistency bound to the abdominal wall. It appeared so likely that I was dealing with some kind of a cyst, that a trocar was inserted, but with no result. The anterior adhesions were broken up, only to find that still stronger adhesions bound the tumor to the intestine. These were in turn torn apart and the pedicle ligated. But before doing so it was discovered that the pedicle was twisted and the splenic artery completely occluded. The abdomen was then washed, filled with sterile water, and closed.

Mrs. E. remained in the hospital some six weeks. Aside from the development of an intermuscular abscess (and a consequent

fever) the convalescence was almost uneventful. A second rise of temperature yielded to quinine, probably showing a latent malaria. An attack of intestinal indigestion toward the end of convalescence caused some disturbance; this, however, was not repeated. Bland Sutton states that it is a fact that many if not all individuals with wandering spleens are very thin and often gaunt, and so far as his observations go they retain this character when spleenless. Mrs. E., on the contrary, while a small woman, showed no signs of emaciation, and a letter from her husband a month after her return, assures me that she has gained in weight twenty pounds. Six weeks after her return she weighs one hundred and fifteen pounds, assists Mr. E. with his business, and is getting fat.

The tumor presented an elliptical appearance, being 19 cm. (seven and a half inches) in length, by 10.5 cm. (four and a quarter inches) broad, and 10.0 cm. (four inches) in thickness, of a gelatinous consistency, and dark brown in color. The capsule refused to strip, was greatly thickened, and measured 1 cm. On cross-section several soft spots were found near the hilum. These appeared necrotic, easily washing away. The pulp itself bulged greatly, showing that the capsule was under considerable pressure. The weight of the spleen is variously given by the different authorities as from 150 to 250 grams. This one weighed 700 grams (one and a half pounds). It was removed none too soon.

The microscopic examination revealed several old hemorrhages, as well as a large amount of pigment scattered throughout the mass. The sloughing pulp proved to be necrotic, the tissue refusing to take a basic stain, and staining but poorly with eosin. No nuclei or leukocytes were found; the Malpighian bodies were scarcely visible. The investing envelope showed a division into three layers; an outer fibrous (formed from the peritoneal attachment), a mass of dense fibrous tissue (the original capsule with some hypertrophy), and a third formed of a greatly enlarged and dense network (the old trabeculae) filled in with young connective tissue. In other words, there was a subacute inflammation of the capsule, a chronic passive hyperæmia of the pulp, and a well-advanced necrosis. So far as I know, there is no description of this method of capsular hypertrophy in our text-books, and it therefore seems well to lay a special emphasis upon the condition here noted.

A careful examination of all the available literature since 1890, while showing perhaps 150 removals, gives only 22 operations on cases of wandering spleen. Of these only 8 (the cases of Sutton,<sup>1</sup> 1892; Hertaux,<sup>2</sup> 1893; Malin,<sup>3</sup> 1894; Runge,<sup>4</sup> 1895; Chandleux,<sup>5</sup>

<sup>1</sup> Transactions of the Clinical Society of London, 1892-1893, vol. xxvi. pp. 46-49.

<sup>2</sup> Bull. et mém. de la Soc. de chir. de Paris, 1893, n. s. tome xix. p. 752.

<sup>3</sup> Lancet, London, 1894, vol. ii. p. 627.

<sup>4</sup> Berl. klin. Wochenschr., 1895, Bd. xxxii. p. 346.

<sup>5</sup> Bull. de la Soc. de chir. de Lyon, 1899-1900, tome iii. p. 92.



and Stengel,<sup>1</sup> 1899; Bennett,<sup>2</sup> 1900, and Webster,<sup>3</sup> 1903) had a twisted pedicle. Of these 8, Webster's and Bennett's cases were attended with a necrosis, though only one (Webster) mentions an adhesion. But assuming that several of the 8 reported since 1890 were complicated by adhesions or necrosis, my own case is the ninth.

My thanks are due to Dr. J. M. Newbern, of Jarvisburg, N. C., for the history of the case; to my associate and consultant, Dr. H. M. Nash, of this city; and to Drs. H. S. Baker and W. C. Campbell, of the Norfolk Protestant Hospital, for their many courtesies.

## RECENT ADVANCES IN THE TECHNIQUE OF ROENTGEN-RAY THERAPY.<sup>4</sup>

BY CHARLES LESTER LEONARD, A.M., M.D.,  
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THE great variance in the results reported in the treatment of disease by the Roentgen method must strike the reader of medical literature very forcibly and lead him to wonder if there is any truth in the favorable reports, or any logical explanation for the diversified and often apparently antagonistic physiological effects.

This feeling of doubt is readily enforced if he has chanced to come in clinical contact with the results of an inexperienced operator. It must, however, be remembered that positive evidence is always more valuable than negative. That even a few accurate observations of beneficial results attained are far weightier evidence of therapeutic efficiency than any number of failures. The time has not yet arrived when cures can be demonstrated; a longer period of therapeutic employment is necessary, though many cases have remained apparently cured for over two years. An inhibitory action has, however, been absolutely demonstrated. The power to inhibit the growth of malignant or other pathological cells has been demonstrated beyond question. This agent has been proved to be more potent than any other agent heretofore employed in checking the growth of malignant cells. Even operation, which was the most effective method of treatment, does not inhibit the growth of disease; it eradicates it by removing it from the body, but in no way alters the nature or character of the cellular growth.

<sup>1</sup> American Surgery, Philadelphia, 1899, vol. xxx. p. 321.

<sup>2</sup> Texas Medical News, Austin, 1900-1901, vol. x. p. 703.

<sup>3</sup> Journal of the American Medical Association, Chicago, 1903, vol. xl. p. 887.

<sup>4</sup> Read before the College of Physicians of Philadelphia, February 1, 1905.

Operation is not curative except by being destructive; the Roentgen ray has been demonstrated to have inhibitory power over the cellular malignant activity of new-growths; it is reconstructive rather than destructive.

While the failures to secure permanent results far outnumber the successes, they do not outweigh them. The Roentgen method has been too frequently asked to accomplish results that were impossible by other means, and hopeless cases have been the rule rather than the exception. When it has had the opportunity to co-operate in treating cases after surgical removal of the focus of malignant disease, the results obtained in the treatment of these conditions will be improved. Roentgen treatment should supplement but never supplant operation, where operation is admissible. But to attain the highest degree of success, cases must be sent early for Roentgen treatment, as well as early for operative intervention.

The apparent variation in the effect of the Roentgen rays on disease is to be explained by differences in the technique employed by operators, and by inefficient employment resulting from inexperience and the timidity which it breeds.

The prevailing idea that this method of treatment is successful in and can only hope to influence superficial malignant growths is erroneous. The rarity of cases in which it has affected deep-seated growths has been due to lack of knowledge of the qualities of Roentgen rays suitable for their treatment and defective technique and experience in employing them. There are enough authenticated cases to demonstrate its power, and recent advances in the knowledge of technique has placed them more readily under the influence of this agent.

The facts already demonstrated make it the most potent alterative and curative agent known for the treatment of malignant disease. They make it imperative that every conscientious practitioner should carefully consider the employment of this agent as a supplementary method to surgical operation in the treatment of every case of malignant disease that comes under his care. The mortality from malignant disease even after early radical surgical removal is so great that so powerful a supplementary method of treatment ought not to be neglected.

A review of the probable physiological action and pathological changes that follow its employment will in a measure explain the rationale of its wide field of application and harmonize its apparently antagonistic effects. A study of the principles that underly its application will help to a realization of the difficulties that must be mastered by technique before accuracy and efficiency in dosage can be expected. The variation in results can then be more readily understood and can be shown to follow defective technique and not to be due to the valuelessness of the agent. It will be easy to

appreciate why results can be obtained by those possessing technique and experience, while others fail even to improve similar cases.

A reasonable deduction regarding the physiological action of this agent can be gained from the clinical observation of its effects. Stimulation of nutrition, both local and systemic, has been almost universally observed where physiological effects have been produced. Changes due to altered metabolism are seen in all cases and pathological examinations have repeatedly demonstrated varying degrees of retrograde metamorphosis in tumors that have been effectively treated. This stimulant action when pushed produces decided alterative effects, which have been ascribed to the autolytic ferments within the cells and results finally in their dissolution and absorption. The effect of these forces, fortunately, is varied in its action on normal and pathological cells, a result not uncommon to stimuli. The stimulus which will injure pathological cells has no harmful effect upon normal metabolism, but rather increases the vitality and growth of normal tissues. This hypothesis readily explains the selective action of the Roentgen treatment and shows why effective dosage is difficult, since it must be strong enough to injure pathological cells and yet not too strong for normal tissues. Fortunately in practice the reaction of the skin forms a valuable clinical guide.

The clinically demonstrated physiological action of this agent, whatever it really may be, is at least unique, since it possesses the power of inhibiting the growth of malignant cells, possibly of destroying them. No other agent has ever demonstrated such power over the morbidity or the cellular energy of growth of malignant tumors. No other agent has possessed the selective power to destroy malignant cells without injuring the normal surrounding structures. The only effective method of treatment has been the removal of the diseased tissue with the surrounding normal structure or their total destruction *in situ* by cauterants. The great difference between this and all other agents employed in treating malignant disease is that it differentiates between pathological and normal tissues, retarding and preventing the development of pathological cellular activity, while it does not harm or hinder the growth of normal cells.

The latest views regarding malignant growths attribute their malignant character to an inherent and unexplained increase in the energy of growth of their cells, which experimental studies (Loeb) have shown is in marked contrast to that of the cells of normal tissues or of benign tumors. This energy varies in intensity in different tumors, but is constant for each tumor even through a long series of transplantations. Further, it has apparently been demonstrated that the formation of metastases is caused and can occur only where there is a primary increase in the energy of growth of the tumor cells.

These pathological facts harmonize with the physiological action attributed to the Roentgen energy. In their light the rationale and value of preparatory or tentative Roentgen treatment before operation and of postoperative treatment can be seen. The peculiar primary energy of growth of malignant cells is reduced by the inhibitory action of the rays. The growth not only of the original tumor but also of metastases and wandering malignant cells is checked.

It is generally conceded that an irritating or exciting cause is an essential to the development of malignant growths, and that often incomplete operations act as exciting causes and increase the morbidity of the growth. Preparatory and postoperative treatment are, therefore, valuable, because they inhibit the energy of malignant cells, if they do not destroy them, and render metastasis less liable, while the supplementary treatment destroys any remaining cells or inhibits their growth.

Can it be possible that in these pathological findings and physiological action an explanation is found for the production of malignant growths in the hands of Roentgen operators? Such cases have, unfortunately, been reported, and in them the disease originated simultaneously in both hands. Possibly the continued though feeble stimulation of normal cells resulted in a permanent increase in their energy of growth, whereby they took on the characteristics of malignant cells and acquired the power to grow and multiply at the expense of surrounding normal tissues and to form metastases.

An analogous process as diametrically opposed as is the destruction and production of malignant disease is seen in the clinical effects in hirsuties and alopecia areata, where overstimulation destroys the hair and mild stimulation causes an increased metabolism in the hair follicles and a renewed growth of hair.

But what are the difficulties that underly the accurate application and dosage of this agent? Why have the results been so varied and antagonistic? Why should they be better? And what is essential to its efficient and successful application?

The chief difficulties that underly the accurate application and dosage of this therapeutic agent lie in its method of production and the variation in its qualities, that must be recognized and applied accurately to be effective. The complicated physical apparatus employed in its production must be thoroughly understood, and special knowledge and technique acquired to produce and recognize the various qualities of this therapeutic force. In addition, clinical experience and knowledge are essential to an appreciation of their effects and the adaptation of the particular quality of energy to the lesion which it most readily affects.

Improvements in apparatus for the production and measurement of the amount of energy that is developed make these difficulties less and the acquirement of technique easier; but there will always

remain the problems common to the employment of all remedies in clinical work. As has been aptly said of this agent, it must be applied in the proper quality, dose, and frequency. The most specific drugs known, quinine and mercury, cannot be successfully applied without accurate diagnosis and the help of clinical experience in dosage.

With the necessity of developing special technique to produce this therapeutic agent accurately, and again clinical technique and experience in employing it, is it to be wondered at that results have been often disheartening to those who have expected any quality and any dose to accomplish results? When, in addition, it is remembered that the majority of cases treated, especially of malignant disease, have been hopelessly inoperable, is it not a proof of the inherent value of this agent that any successes have been recorded?

The recognition of the necessity of adapting the quality and dose of this agent to each individual lesion and patient, and a clearer knowledge of which quality and technique is applicable to each group of cases, afford the prospect of greater developments and of more frequent successes in the future.

Efficient Roentgen therapy is not the result of chance, nor can it be purchased with the apparatus. The wonderful results that have been produced, though they may not be always repeated, were not due to good fortune or accident. They have followed diligent, untiring study of the phenomena observed in the Roentgen tube and their clinical effects upon disease. The necessity for special education of the clinician who would apply this agent effectively is self-evident. The knowledge of how to produce the required quality of Roentgen discharge must be combined with the knowledge of when to apply it, and clinical experience must be capable of measuring the exact dose. No therapeutic agent can be effective without the fulfilment of these requirements, and there is little wonder that without them more failures than successes have been recorded.

Such a powerful therapeutic agent is dangerous or useless in the hands of anyone less well qualified. It is dangerous if he employ it in a dose capable of doing good and is incapable of accurately observing its effects; and it is useless and even harmful if inexperience makes him timid in its employment, or ignorance leads him to employ a dose that will stimulate instead of injure pathological tissues.

But are not the poor results in deep-seated disease due to the limitations of this therapeutic agent, or why is it that so many can produce effects upon superficial lesions and cannot influence the deep-seated? There was a similar condition in the field of Roentgen diagnosis; at first lesions of bone in fingers, hands, and toes only could be diagnosed; as technique improved all parts of the body have been penetrated and the various tissues have finally yielded

to a differentiation in their shadows. Those who can produce therapeutic effects on superficial lesions only will often be found as defective in making diagnoses of deep-seated lesions. Any technique and any even inefficient apparatus will effect superficial lesions just as they will make pictures, and some diagnoses in the bones of the hand and arm. The progress which has marked the development of improved technique in Roentgen diagnosis will find its counterpart in Roentgen therapeutics. The effects of varying qualities of Roentgen rays in therapeutics is now being studied as were their effects upon diagnosis. There is a more accurate application and greater efficiency already manifest. Three years ago it took twenty-eight treatments to cure an epithelioma of the eyelid which has remained cured since. A similar growth was removed apparently as effectively this winter in fourteen treatments. The result was due to an improved technique and an adaptation of the fitting quality of ray to the disease. The qualities peculiarly adapted to each variety and situation of disease are being gradually determined; many of them are already known. Advances and better results have followed and will follow each improvement in technique.

The means for measuring the amount of energy flowing through the tube have been improved, so that it is possible to compare the technique of different operators more accurately and to determine in what the effective treatment for each lesion consists.

When and how should this therapeutic agent be applied to make it most effective and of the greatest benefit to the patient?

In malignant disease it should undoubtedly be employed in conjunction with operation, not as a substitute for it, but as a component part of the treatment. Up to the advent of the Roentgen method of treatment early radical surgical removal of so much of the diseased tissues as was possible was the most efficient treatment known. That, however, cannot be as truly said now. The efficiency of the Roentgen treatment has been demonstrated to be great; it is capable of modifying the malignant nature of the cells, retarding their growth if not totally destroying them. Surgery cannot, therefore, be said to be the most efficient treatment unless it is combined with thorough postoperative Roentgen treatment.

Surgical operation and Roentgen treatment are not antagonistic, but mutually helpful and supplementary, and the patient's greatest good can be served only when they are combined. The time for applying the Roentgen rays should be either immediately after operation or just before, as a short preparatory treatment to reduce the energy of growth of the cells and destroy the outlying cells, and then again after operation.

The patient has the best chance of permanent relief from malignant disease who is brought early for operation, and that operation followed immediately by a thorough course of Roentgen treatment

The treatment must be as severe as the patient can stand, both locally and through the systemic effects, if it is to be of value.

A marked dermatitis or tanning of the skin must be produced or sufficient severity in the dose has not been employed. Auto-intoxication from the absorption of the dissolved malignant cells must be expected if efficient dosage has been employed where there are large growths. In cases where treatment is efficient this auto-intoxication will manifest itself in rheumatic pains in muscles and joints, disturbances of the stomach and liver, and a general feeling of malaise. The detection of these symptoms is an indication for the interruption of treatment for one or two weeks, as its continuance would put the patient in bed. It is, however, an indication of effective treatment. Such symptoms can, however, be produced only where there are large masses of tissue of low vitality that can be affected, as in massive recurrences or inoperable growths. It is to obviate this absorption and to hasten treatment that palliative operations can be employed in practically hopeless cases before the Roentgen rays are used. The inhibitory action, together with the ability to relieve pain where nerve trunks are not involved in the disease, makes the Roentgen rays the most potent palliative remedy known in the late stages of malignant disease.

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## A CASE OF UNIVERSAL CONGENITAL ATRICHIA.

BY AUGUSTUS A. ESHNER, M.D.,  
OF PHILADELPHIA.

THE unique case I am about to report is one of total absence of hair from all parts of the body, existing, so far as could be learned, from birth. If the history, as given by the patient, is correct, the condition cannot, strictly speaking, be regarded as one of alopecia or baldness, that is, loss of hair, but, rather, as one of atrichia, namely, failure on the part of the hair to develop. The universal distribution of the disorder is not the least remarkable feature. In addition, the nails exhibited significant changes, and there was present, besides, the rare anomaly of retinitis albicans.

The patient was a house-painter, aged sixty-four years, who was admitted to the Philadelphia General Hospital on January 2, 1904, complaining of pains throughout the body, especially in the lumbosacral region. He presented slight swelling of both lower extremities and drooping of the right upper eyelid, with inability to elevate the lid properly. The action of his heart was arrhythmic, but the sounds were clear. The especially noteworthy feature about the patient was the total absence of hair from all parts of the body, a

condition that, according to the patient's repeated statement, had existed from birth. The skin itself was soft, smooth, and unctuous. The man related, further, that he perspired but little. The nails of the fingers and toes were only about one-half the normal length, and their distal extremities were irregular and longitudinally rugous. The patient stated that they had presented this appearance from birth and that he never trimmed them. He had only three teeth in the lower jaw and none in the upper; the others had gradually fallen out in the progress of time. The urine was free from albumin and sugar.

Dr. C. A. Oliver kindly examined the eyes and confirmed the absence of lashes. In addition, he found the condition of retinitis albicans, characterized by the presence of numerous mosaics and areas of whitish masses, with exposure of the underlying sclerotic. So far as the patient knew, no other member of his family exhibited a like absence of hair or alteration in the nails. He gave a personal history of gonorrhœa and of lead poisoning; there was some doubt as to syphilis.

The accompanying illustrations show the absence of hair from the head and the face, including eyebrows and eyelashes. Negatives obtained from exposure of the entire body, and of the hands separately to show the finger-nails, proved unsuccessful, and the patient declined to be exposed again.

Whether the absence of hair in this case had really existed from birth, as the patient maintained, cannot, of course, be established with certainty, as we have only his unconfirmed statement to this effect. In any event, the condition, whether one of generalized loss of hair or one of generalized failure on the part of the hair to develop, is exceedingly rare. I have been able to find records of only a few similar cases, and to some of these the references are exceedingly brief, and in some instances indefinite.

F. G. Danz<sup>1</sup> refers briefly to two grown brothers who had always presented entire deficiency of both teeth and hair.

Steinmig<sup>2</sup> reports the cases of a boy, aged three and a half years, and his sister, aged one year, whose bodies at birth were devoid of hair and covered only with vernix caseosa. Nowhere on the head was there even a trace of lanugo, and eyebrows and eyelashes alike were absent. The nails of the fingers and toes were only indicated, appearing as shrunken or shrivelled points. The children sweated freely, especially about the head. The parents were healthy and had each a strong growth of hair.

John F. South<sup>3</sup> refers to the case of a man, aged twenty years,

<sup>1</sup> Stark's Archiv f. die Geburtshülfe, Frauenzimmer- und Neugebörner Kinderkrankheiten, Bd. iv., 3. Stück, Jena, 1792, p. 684.

<sup>2</sup> Notizen aus dem Gebiete der Natur- und Heilkunde, Bd. xxvi., No. 4, November, 1829, No. 554, p. 50.

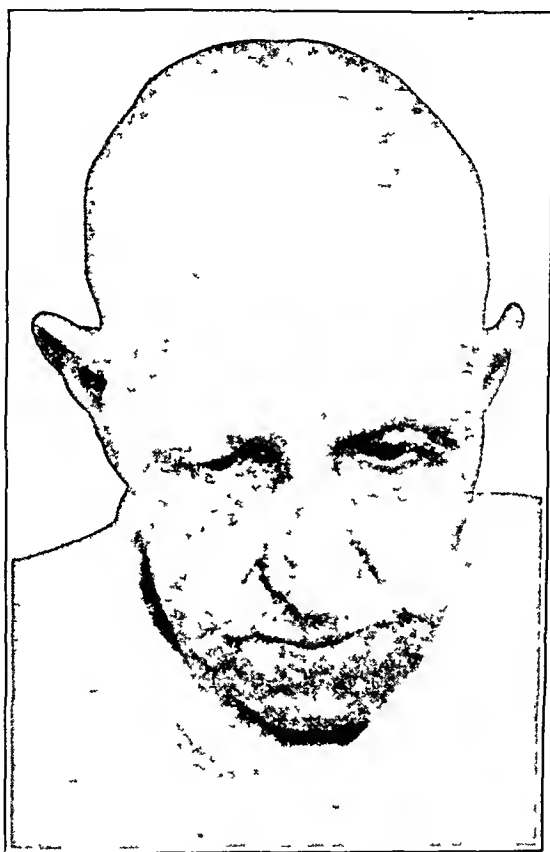
<sup>3</sup> Translation of Adolph Wilhelm Otto's Compendium of Human and Comparative Pathological Anatomy, London, 1831, p. 120.



who had no hair on his head, eyebrows, eyelids, or chin, and was said to have none on the pubes.

Burkard Eble<sup>1</sup> cites Laurent Heister,<sup>2</sup> as speaking of two individuals that had no hair on the entire body; and as having seen a man, aged about forty years, and otherwise well, who, some ten years previously, had, without recognizable disease, lost all of his hair, including the eyebrows and eyelashes, so that no trace could be discovered; and also a woman, who, without antecedent

FIG. 1



Universal congenital atrichia, front view.

disease, had lost all of her hair. He refers to observations of individuals without hair or teeth recorded in the *Transactions of a Society of London* for 1800, and the *Salzburger medicinisch-chirurgische Zeitung* for 1801, vol. i. p. 250; quotes Schenk as authority for the statement that King Louis of Hungary was born without

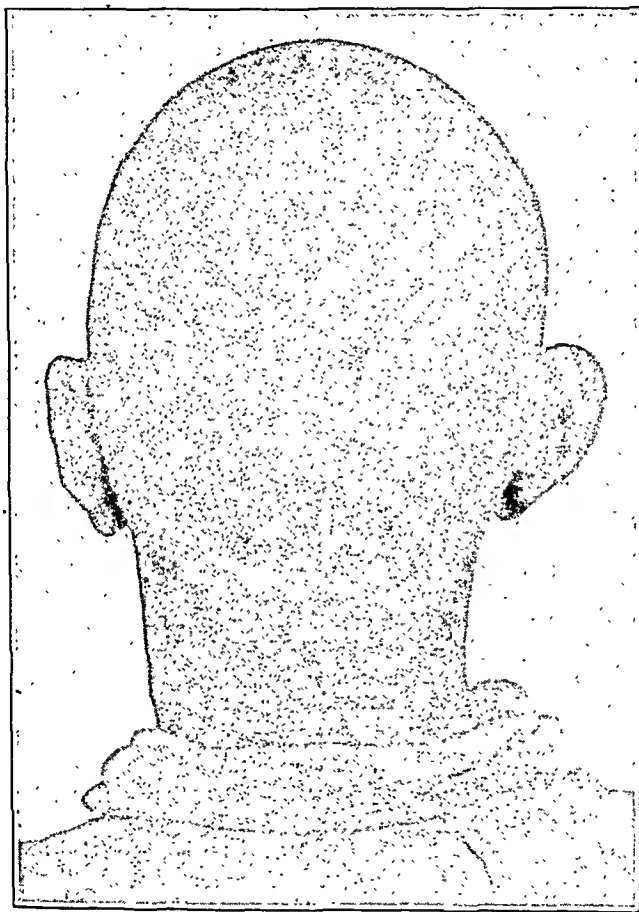
<sup>1</sup> Die Lehre von den Haaren in der gesamten organischen Natur, Vienna, 1831, Bd 11, p 244

<sup>2</sup> Medicinische, chirurgische und anatomische Wahrnehmungen, Rostock, 1753

hair; cites the observation by Dr. Wells<sup>1</sup> of similar complete absence of hair, by H. F. Delius of an individual without even the smallest hair upon the body, and by Augustin<sup>2</sup> of a man on whose body no trace of hair could be observed; and speaks of a similar case mentioned by Leveling.<sup>3</sup>

M. Schede<sup>4</sup> has reported the cases of a brother and sister, aged thirteen years and six months respectively, who were hairless at birth and continued to be so up to the time of observation, when no

FIG. 2.



Universal congenital atrichia; back view.

trace of hair could be discovered on any part of the body. The parents and two other children intermediate in age were healthy and exhibited a full growth of hair. A piece of scalp was excised from the head of the elder of the children in question, and well-

<sup>1</sup> Transactions of a Society for the Improvement of Medical and Surgical Knowledge, 1800, vol. ii.

<sup>2</sup> Asklepieion, March, 1812, Heft 3.

<sup>3</sup> Haller's Grundriss der Physiologie, Erlangen, 1795, Bd. viii., p. 1. Theil, note 325, p. 384.

<sup>4</sup> Archiv f. klinische Chirurgie, 1872, Bd. xiv., p. 158.

developed, sebaceous glands were found opening on the surface, while at their base were sebaceous cells having distinct nuclei and fragmented contents. Nearer the orifice the cells formed irregular sebaceous masses. Close by were a large number of small and large atheromas separated from the glands by connective tissue, evidently developed from glandular tubes. All of the latter, however, were not distended or degenerated. In places they were short and straight or slightly convoluted and not always provided with a lumen. They were filled with cells arranged in two layers, an outer, consisting of long, narrow cylinders, with rod-shaped nuclei, and an inner, consisting of small, round, or polygonal cells. These were looked upon as rudimentary hair follicles. The sweat glands were not normally developed. The erector muscles of the hair were well developed, but there was no sign of hair.

J. Higham Bell<sup>1</sup> refers to an aboriginal black man and woman, brother and sister, said to be entirely devoid of hair, a sister of whom, similarly hairless, had died a few years before, and who had, when young, been brought to a station in Australia in the same hairless state. They were thought to belong to a tribe of hairless Australian blacks. Photographs represented a well-formed and well-developed man and woman of middle age, without a particle of hair visible on their heads and bodies, and none was found on most careful inspection. The peculiarity is especially striking, as the Australian aborigines are naturally a hairy race.

In a paper on so-called dog-men, Alexander Brandt<sup>2</sup> refers to a Russian peasant with absolute congenital atrichia mentioned by one of his students. He points out that the fetal lanugo may either fall out and not be replaced by permanent hair or be excessive and persistent, and give rise to the condition of abnormal hairiness.

An additional number of cases have been reported in which there has been temporary or transitory absence or loss of hair, generalized or local, natal or postnatal, often in conjunction with abnormal conditions of the nails and the teeth, sometimes with deficiency or total absence of perspiration; in one instance with absence of the secretion of tears, and in one with absence of the mammary glands; frequently there was a familial distribution.

Rayer<sup>3</sup> reports the case of a man whose cranium appeared entirely naked, although, on close examination, a quantity of fine, silky, white down was found present. There were also a few black specks on the temples representing stumps of hairs that had been shaved off. The eyebrows were indicated by fine short hairs. The edges of the lids were without lashes, but the bulb of each of these was indicated by a small, whitish point. The beard was thin and weak. There were

<sup>1</sup> British Medical Journal, January 29, 1881, p. 177.

<sup>2</sup> Biologisches Centralblatt, March 1, 1897, Bd. xvii., p. 161.

<sup>3</sup> Theoretical and Practical Treatise on Diseases of the Skin, second edition, translated by R. Willis, London, 1835, p. 1049.

a few straggling hairs on the breast and pubic region, and scarcely any in the axillæ. Hair was more abundant on the inner aspect of the legs. The father of the patient presented a similar defect.

John Thurnam<sup>1</sup> has reported two cases in cousins exhibiting imperfect development of skin, hair, and teeth. One occurred in a man, who died at the age of fifty-eight years, and was, during life, almost completely without hair. He had only four teeth. There was a small amount of fine hair on the head and face, in the axillæ, and on the pubes. The eyebrows were absent, and the eyelashes were defective. The skin generally was fine, thin, and delicate, and its surface was often dry and harsh, without traces of sensible perspiration and any trace of unctuousity. Sudorifics made the skin soft and relaxed, but had no effect upon its state of moisture. A trace of fluid appeared upon the surface in the last week or ten days of life. There was, further, an absence of tears. After death the skin was found in a condition of atrophy and atony, and the sudoriparous apparatus defective. The second case was in a maternal cousin who exhibited almost precisely the same peculiarity, the head being equally bald, the skin similarly delicate in structure, the sensible perspiration and tears likewise absent, and the teeth also deficient. The maternal grandmother exhibited extreme delicacy of the skin, with a limited amount of sensible perspiration.

In discussing Thurnam's case, Williams<sup>2</sup> referred to the case of a girl, aged fifteen years, described as being devoid of hair and teeth, but found to be not entirely so. The hair was fine, scanty, and white, although there was scarcely any forming the brows and lashes. The patient had three or four projections resembling teeth, and these were carious. She had never perspired, and menstruation had not yet set in.

William Sedgwick<sup>3</sup> cites the case, reported by T. H. Burgess, of a boy, aged eight years, who was without a vestige of hair on the scalp, devoid of eyebrows and eyelashes, and without hair on any part of the body. He had the usual supply of hair until the age of four years, when it began to fall out gradually, until it had disappeared entirely. The brother of this boy, two years younger, had begun to lose his hair in detached places. His sisters, younger and older, had a good supply of hair, as had also the parents.

H. MacNaughton Jones and Ringrose Atkins<sup>4</sup> describe the microscopic appearances in a case of so-called congenital alopecia. The patient was a boy, under treatment for his eyes, who had no recollection of ever having had any hair on his scalp, although he had heard during youth of the presence of some downy hairs. The face was the only part of the body on which there was any appearance of

<sup>1</sup> Medico-Chirurgical Transactions, 1848, vol. xxxi., p. 71.

<sup>2</sup> London Medical Gazette, 1848, vol. vi., p. 336.

<sup>3</sup> British and Foreign Medico-Chirurgical Review, 1863, vol. xxxi.

<sup>4</sup> Dublin Journal of Medical Science, 1875, vol. lx., p. 200.

hair, and here there was a fine down. The finger-nails were aborted and badly formed, with ridges and furrows. The teeth were irregular, far apart, and marked by transverse ridges and discoloration. Histological examination of sections of the scalp disclosed the presence of irregular tubules, crossed by fine trabeculæ, and containing granular material, and also in places an aggregation of circular and ovoid apertures deeply lined with small and compressed epidermic cells. These apertures appeared to be transverse sections of tubular cylinders, and these were thought to represent hair follicles altered in situation, position, and structure. Here and there was an aborted hair follicle, forming a shallow pit in the epidermic layer and lined by a layer of similar cells, the open extremity looking downward.

J. B. Luce<sup>1</sup> reports the case of a girl, aged eight and one-half years, who was said to have been entirely bald at birth. In the sixth month a number of small elevations appeared on the scalp, and the first hairs were observed at the age of six years. At eight and one-half years numerous lanugo hairs were present, and also a little blackish-gray hair. The scalp was the seat of conical nodules, the skin over which presented a normal color, with a central dark point. Introduction of a needle into such a nodule permitted the escape of a rolled-up hair.

Paul Michelson<sup>2</sup> cites the case of a girl, aged two years, otherwise normal, whose head was sparsely covered with lanugo.

S. H. Guilford,<sup>3</sup> of Philadelphia, describes the case of a man, aged forty-eight years, edentulous from birth, who exhibited absence of the sense of smell, almost complete absence of the sense of taste, absence of sweating and of hair from the trunk, with an excess of hair on the face, in the axillæ, and in the pubic region, while the head was covered with soft down. His maternal grandmother had never had hair or teeth, while his mother was normal in these respects. A brother of the latter also was without teeth and hair. Of her twenty-one children, eighteen were living, but the patient was the only one without teeth, although in some certain teeth had failed to make their appearance. The patient himself had eight children, several of whom were in some degree edentulous, although otherwise normal.

Jonathan Hutchinson<sup>4</sup> has reported a case of congenital absence of the hair and the mammary glands in a boy aged three and one-half years. The head, however, was covered by a quantity of down, and the teeth were normal. The nails of the fingers and toes were thin and curved backward, presenting a depression in the middle. The nipples were replaced by cicatricial patches, but there was no

<sup>1</sup> Thèse de Paris, 1879, No. 579; Schmidt's Jahrbücher, Bd. exci., Heft 1, p. 31.

<sup>2</sup> Handbuch der Hautkrankheiten in Ziemssen's Handbuch der speciellen Pathologie und Therapie, Leipzig, 1883, p. 107.

<sup>3</sup> Wiener medizinische Wochenschrift, 1888, No. 37, p. 1116.

<sup>4</sup> Medico-Chirurgical Transactions, 1886, vol. vii. p. 478.

trace of the mammary glands. The mother had, from the age of six years to the time of the report, suffered a gradual loss of hair from alopecia areata. At first the scalp became bald and smooth; subsequently the eyebrows and eyelashes fell out. The latter grew again, and a few tufts of hair appeared on the scalp.

This case has been more recently described by Hastings Gilford<sup>1</sup> as one of progeria, or premature senility. The patient was at that time fifteen and one-half years old. On close inspection a feeble growth of colorless hair was found on the back of the hands and wrists and on the head. The teeth were of good size and in fair condition. In another case, reported by Gilford,<sup>2</sup> the patient was a young man, aged eighteen years, whose eyebrows and eyelids at first appeared devoid of hair, but on close inspection a few scattered and downy hairs were discovered in both situations. A small number were detected also on the backs of the hands and wrists. None, however, could be found upon any other part of the body. The nails of the fingers and toes were short, ill-shaped, and membranous.

Paul de Molènes<sup>3</sup> reports the case of a girl, aged four and one-half years, who at birth presented an almost imperceptible down on the scalp, scarcely developed eyelashes, and normal nails, with an absence of eyebrows. At the age of five months the eyelashes fell out, and at the age of sixteen months the entire hairy system was deficient. On the scalp no down was visible, even with the aid of a lens, although numerous orifices were present, indicative of the integrity of the pilosebaceous organs. A fine white down was discernible on the lower lids with the aid of a lens. The nails and teeth were normal. Under treatment slow and gradual growth of hairs took place in various situations. Hairs and follicles were found normal on microscopic examination. The mother of the patient had been treated for extensive alopecia areata at the age of nineteen years, and a brother at the age of six years.

Molènes states that the condition of atrichia is exceedingly rare and almost never absolute. Generally a fine down is present, indicating the existence of hair follicles. Usually, also, the anomaly is partial. It may persist for several months after birth, and even up to the second year. Few examples are known in which it persisted throughout life. Molènes considered it a perversion of function or an arrest of development affecting the organ giving rise to the hair.

Two cases of congenital familial alopecia were exhibited at the meeting of the Société Française de Dermatologie et de Syphilographie, held November 10, 1892. The condition could not have been complete, as the statement is made that the hair was the seat of a garland-like malformation.<sup>4</sup>

<sup>1</sup> Practitioner, August, 1904.

<sup>3</sup> Annales de dermatologie et de syphilographie, 1890, tome i., p. 548.

<sup>4</sup> Monatshefte f. praktische Dermatologie, 1892, Bd. ii., p. 618.

<sup>2</sup> Ibid.

Aubry<sup>1</sup> reports a case of congenital alopecia in a young man, aged sixteen years, in which the loss of hair followed, in a general way, the lines of the cranial sutures, the remainder of the head being covered with a dense layer of black hair.

The condition was thought to be due to atrophy of the skin from stretching, in consequence of hydrocephalus. The teeth were normal.

At a meeting of the New York Dermatological Society, held November 27, 1894, J. A. Fordyce<sup>2</sup> presented a girl, aged four years, with complete alopecia. A few hairs were noticed at birth, but these soon fell out. A few scattered eyelashes were present. There was no family history of alopecia.

P. S. Abraham<sup>3</sup> reports three cases of congenital alopecia in a mother and her two children. The former, aged thirty-three years, exhibited complete absence of hair from the eyebrows, eyelids, arms, legs, trunk, with a scanty supply on the scalp, pubes, and axillæ. At birth there was a small fluff on the head, but this soon fell out. The absence of hair remained complete until the age of eighteen years, when hair gradually made its appearance on the scalp, in the axillæ, and on the pubes. Of the children, one, aged five years, was in a state of almost complete alopecia. There was a little down on the head at birth, but this fell out at the age of three months. The second child, aged fifteen months, likewise appeared to be completely without hair. It had black hair at birth, but this fell out at the age of three months.

C. Nicolle and A. Halipré<sup>4</sup> have described a condition of deficiency of the hair, with trophic changes in the nails, occurring in thirty-six members of one family during six generations. He reports at some length the case of a young man, aged eighteen years, deficient mentally, whose eyebrows were scanty and unpigmented, the lashes white, the hair on the scalp thin and in places lighter in color than elsewhere. There was no hair on the anterior aspect of the chest, only a few short, white hairs in the axillæ, no mammary hair, and a moderate amount of long brown hair on the pubes. The teeth were normal. The terminal phalanx of each finger was larger than normal, œdematous and red, while the nails were in varying degree hypertrophied, longer and thicker than normal, rugous and scaly, with a tendency to become elevated and incurvated at the extremity. The majority exhibited exaggeration of the longitudinal striation, and some were striated transversely. They were extremely friable, some being cracked in the middle and others longitudinally. Some were separated and tended to become detached. The free border was, in general, black, the rest of the nail grayish-yellow. The

<sup>1</sup> *Annales de dermatologie et de syphilographie*, 1893, 3. ser., tome iv., p. 899.

<sup>2</sup> *Journal of Cutaneous and Genito-Urinary Diseases*, vol. xiii., p. 120.

<sup>3</sup> *British Journal of Dermatology*, 1895, vol. vii., p. 162.

<sup>4</sup> *Annales de dermatologie et de syphilographie*, 1895, 3. ser., tome vi., p. 804.

extremities of most of the fingers about and beneath the nails were the seat of ulceration.

A case of similar character is reported by Charles J. White.<sup>1</sup> This occurred in a young man, aged nineteen years, who presented an abundant uniform growth of pale, short, downy hair on the scalp, with an absence of hairs from the cheeks, the chin, and the axillæ. The eyelids and eyebrows were normal, the hair on the upper lip of the lanugo type, and a few hairs were present on the pubes. From the age of nine years, following an injury to two of the fingers of one hand, the bed of the nails of all of the fingers and toes was from time to time the seat of ulceration, the nails becoming thickened and broken and discolored at the extremities. *Staphylococcus pyogenes aureus* and *staphylococcus pyogenes* were obtained on culture. The hairs presented a normal appearance. The great-grandfather of the patient had had little hair, and the nails of his fingers and toes were faulty in development. The second generation escaped. The third generation comprised eight children, six sons and two daughters, of whom one son and two daughters were affected—the mother and two uncles of the patient. The former had always had but little hair, and the finger-nails had for years been thickened and abnormal. The uncles had had normal hair, but the nails were bad. One of the uncles married and had two children, a son of nine years and a daughter of four years. The latter was born without hair or nails, and these failed to develop. The patient had one sister, two step-brothers, and one step-sister. The sister had a thick, downy head of hair, the individual hairs being blonde and short.

Paul Ziegler<sup>2</sup> has reported the case of a girl, aged seventeen years, who was hairless at birth, though otherwise normal. She was the youngest of eleven children, all of whom but her presented no abnormality. There was no family history of aberrant growth of hair. From the age of thirteen years a small bunch of black hair made its appearance every four weeks at the occipital protuberance, disappearing in the course of four days with the cessation of menstruation. From the same period, also, there had been a small amount of down on the cheeks. A year previously a few hairs of normal appearance had developed on the eyebrows and eyelids. Recently the patient had noticed fine hair on the forearms. The teeth and nails exhibited no peculiarity. The arms, shoulders, and thighs were the seat of lichen pilaris. On microscopic examination of a bit of skin removed from the scalp, the epithelium and the sebaceous glands were found normally developed, with numerous papillæ, but with an absence of hairs. Near the sebaceous glands, generally at their bases, at a distance from the surface epithelium, were isolated convoluted epithelial tubes, with a large, generally circular, lumen and not communicating with the surface. These

<sup>1</sup> Journal of Cutaneous and Genito-Urinary Diseases, 1896, vol. xiv., p. 220.

<sup>2</sup> Archiv f. Dermatologie und Syphilis, 1897, Bd. xxxix., p. 213.



were lined with from four to six layers of cells, and they were surrounded by connective tissue, near which were unstripped muscular fibres—erectors of the hairs. Similar fibres were present also in the vicinity of the sweat glands, which themselves were normal in every respect. The epithelial tubes were thought to represent the remains of the external sheath of the root of the hair.

Ziegler ascribes the failure of the hair to develop to local alterations in the external sheaths of the root of the hair below the level of the excretory duct of the sebaceous gland. He thinks excessive production of the cells of the sebaceous duct may cause occlusion of the lower portion of the sheath of the root of the hair, resulting in a constriction off of the lowermost portion of the sheath before the papilla has formed. In some instances he believes there may be delayed growth of otherwise normal hair.

Felix Pinkus<sup>1</sup> has reported the case of a boy, aged eight years, who at birth had a growth of hair on the head, especially on the posterior portion. The forehead was bald, but it was not known if there was any hair on the body. At the age of a few months a deposit of crusts formed on the vertex, and this was followed by loss of the hair. The child was quite bald at the age of nine months, and thereafter only a few hairs grew. The body was at this time almost hairless. A year later there were only a few short hairs at the root of the penis, and only a few on the back from the neck to the buttocks. There was scarcely any hair on the arms and on the legs. The face was the seat of abundant lanugo, with a few stray hairs on the forehead and the cheeks, while the lobule of the ear and the tragus were well supplied with hair. The eyelashes were well developed, while the eyebrows were deficient. On the head the hair was scanty, irregularly distributed and short, though requiring cutting from time to time. The hairs were thin, dark, and twisted. The nails were thin, flat, unduly white, and friable at the edges, and their surface was covered with bands converging to the tips of the fingers. The teeth were in process of change, and some had been extracted. The second premolars were wanting, as well as the left lower canine and both outer upper incisors.

Pinkus employs the term hypotrichosis to designate the condition present in this case, contending that the pathological state does not consist in a loss of hair, but rather in deficient growth, the failure occurring at the time when the lanugo or deciduous hair ordinarily is replaced by the permanent hair. The affection would thus be a developmental defect and not properly a disease.

H. Radcliffe Crocker<sup>2</sup> refers to the case of a girl, aged four years, born without hair or nails. The latter began to grow abnormally within a week, the former not for three years. In addition, there was atrophy of the skin generally.

<sup>1</sup> Archiv f. Dermatologie und Syphilis, 1899, Bd. I., p. 347.

<sup>2</sup> Diseases of the Skin. P. Blakiston's Son & Co., 1903.

## PRIMARY CARCINOMA OF THE OMENTUM WITH PERITONITIS CARCINOMATOSA.<sup>1</sup>

BY ARNOLD STURMDORF, M.D.,  
OF NEW YORK.

WHILE it is not unusual to find the omentum involved in malignant disease, either by contiguity or metastasis from adjacent or remote organs, it is rare to find it the site of a primary malignant growth.

Such primary peritoneal cancers have been the subject of much investigation and controversy and there still exists much confusion in terminology as well as in fundamental conceptions as to histogenesis and development.

For obvious reasons the older publications on this subject cannot be utilized in the elucidation of such obscurities from a modern point of view.

Thus, it was formerly accepted that the histological characteristics of primary peritoneal cancers were typically *carcinomatous*, while within the last decades this view has undergone considerable modification.

It became apparent that the primary development of an epithelial growth, in parts in which epithelium does not normally exist as such, is incompatible with advanced conceptions of histogenic and biologic processes.

Consequently the term *carcinoma* applied to such primary peritoneal neoplasms must prove a misnomer and, as a result, either the *primary* nature or the *carcinomatous* type of the cases reported was questioned, so that in 1872 Waldeyer wrote:

"Whereas, before the appearance of Thiersch's work on this subject, cases of primary carcinoma of the peritoneum were described by a number of observers, no reports of such cases have appeared within the last six years."

The reported cases alluded to in this quotation were discarded by Orth as unauthentic and lacking in definite characterizing detail.

Notwithstanding these theoretical contentions, we find, three years later (in 1875), the report of a case of primary carcinoma of the peritoneum published by Quincke; while again, in 1890, the Committee on Morbid Growths of the Pathological Society of London examined and described as carcinoma, a primary tumor of the omentum with numerous metastatic growths in the abdominal cavity shown by West.

Whether these two authoritative cases really demonstrate the heterologous development of primary carcinoma, must remain an open question until definite knowledge is gained concerning the

<sup>1</sup> Presented before the Surgical Section of the New York Academy of Medicine November 4, 1904, with presentation of specimen and microscopic demonstration.

characterizing elements of the group of tumors embraced by the generic term *endothelioma*.

These latter growths, said to arise from the endothelial layer of lymph- and bloodvessels, may so closely simulate carcinoma in microscopic appearance that their endothelial type can be established only by serial sections, locating their origin in or about the lymphatics and bloodvessels.

The exact histological position, however, of such endotheliomata is still in dispute.

They have been regarded as infectious, and Leyden succeeded in isolating a peculiar form of rhizopod from the ascitic fluid of a case of primary malignant peritonitis.

This finding has been corroborated in a number of cases by Nothnagel, Lauenstein, and Schaudinn.

The last proposed the term *Leydenia gemmipara* for these organisms, although their etiological relationship to peritoneal cancer is not at the present time generally accepted.

Delafeld and Prudden describe endothelioma as "a group of tumors which on the one hand are closely related to the sarcomata in genesis and in some cases in appearance, while on the other hand some of them so closely resemble some forms of carcinoma as to be difficult of distinction from them."

This bizarre nature of the histological criteria in these tumors explains the contradiction as to prevalence and frequency found among authoritative reports.

Thus, Glockner, who analyzed the literature on the subject to 1895, states that "primary peritoneal endothelioma is by no means rare," while Nothnagel mentions but two personally observed cases in which the peritoneum was primarily and exclusively involved.

It is possible that the direction of modern etiological research, in relation to malignant growths in general, may ultimately point the way to an elucidation of some of the obscurities thus briefly outlined; in the present instance, however, it is only possible to adhere to the prevalent caption, carcinoma, leaving it to more advanced doctrines to relegate the cases into their proper category.

The history of our case is as follows:

Mrs. E. C., aged sixty-two years, married thirty years, widow eight years; father died of Bright's disease; mother of pulmonary tuberculosis. Patient was normally delivered of three children, the last twenty-six years ago, all of whom died of tuberculous disease. Menstruation began at fourteen and ceased permanently twenty-five years ago. No menstrual or climacteric abnormalities.

Barring a traumatism which resulted in the acute destruction of her left breast twenty-six years ago, her previous history presents no data bearing on her present condition.

For four months an increasing tenderness, with recurring attacks of pain, accompanied the gradual development of a hard mass,

occupying the middle of the right half of the abdomen. The mass grew rapidly, while pain, abdominal distention, dyspnoea, with loss of flesh and strength, developed to a distressing degree. When first examined, in August of this year, the patient presented the following status: A pale, yet fairly nourished woman of medium stature, with normal pulse and temperature; slight dyspnoea. The heart presents evidences of a compensated mitral insufficiency. Lungs normal; abdomen symmetrically enlarged and very tense.

General abdominal tenderness, most marked in the right half, which contains the major part of a hard, quadrilateral mass, the upper border of which can be defined as a nodular ridge extending across the epigastrium from points continuous with the mammillary lines. The lateral borders of this mass converge (the left more than the right) toward its lower pole, which seems to project free into the pelvic cavity. The mass is very hard and presents a rough, irregularly nodular surface.

It is uninfluenced by respiration, is slightly mobile from side to side, and to a less degree in an upward direction. Its upper border is fixed, while its lower free pole could be subjected to ballottement in the excessive amount of ascitic accumulation. Percussion and colonic inflation indicated the presence of intestine between the liver and the upper border of the growth. Spleen not demonstrable. Genito-urinary organs intact and free from involvement. Marked œdema of ankles. Urine normal. Blood shows 60 per cent. hæmoglobin, no corpuscular changes—quantitative or qualitative.

On September 14th, through a four-inch supraumbilical incision, which gave vent to a large quantity of serosanguineous fluid, a mass of infiltrated omentum was removed. Its removal offered no unusual difficulties. The parietal peritoneum was found studded with countless papillary excrescences, presenting hard, flattened nodules, varying in size from miliary dots to a split pea, very hard, yellowish-white in color, and in many instances showing a tendency to umbilication. Each papilla presented a small area of inflammatory margin around its base. Aside of this finding, the most painstaking search throughout the abdominal contents failed to reveal the presence of similar neoplastic formation as a possible primary or secondary focus of the disease.

Although the cancerous nature of the growth was evident at the time of its extirpation, yet the clinical resemblance to some forms of peritoneal tuberculosis, more especially in view of the tuberculous family history, made a positive differentiation impossible until Dr. Schnaper kindly furnished the microscopic evidence of its carcinomatous character, which I beg to submit for your inspection. He also furnished the following report:

"The tumor upon microscopic examination presents the characteristic picture of an alveolar carcinoma. The epithelial cells are varied in shapes. Nucleus stains well. The epithelial masses are

varied in size and shape; the cells fill the alveoli and are in close relationship to one another. The Van Gieson stain failed to reveal any stroma between the cells. The stroma is made up of firm connective tissue and shows infiltration of fat, and in places there is a round-cell infiltration."

Whether true carcinoma or endothelioma, and if carcinoma, whether primary or secondary, the primary focus having thus far eluded our search, will probably remain an open question for the present. The patient made an uninterrupted recovery from the operation. It is now seven weeks since, and she presents no functional disturbance that might point to the possible involvement of a particular organ and is apparently enjoying the results of a symptomatic cure.

While the case thus detailed presents many points for profitable discussion, both practical and theoretical, there is but one phase of which I would speak in closing, and that is the complicating carcinomatous peritonitis mentioned in the title.

The multiple papillary excrescences found studding the parietal peritoneum cannot be interpreted in this case as merely passive metastatic deposits, but represent a type of malignant subacute efflorescence, clinically similar to that which is recognized as occurring in tuberculous and other infectious processes, and productive of profuse serous exudation. As a matter of fact, such forms of primary acute miliary carcinosis of the peritoneum are described by Bauer in *Ziemssen's Cyclopædia* and by Nothnagel, the miliary excrescences resembling those described above in every detail. In no other way can we explain such enormous ascitic accumulation in so short a period in the absence of circulatory obstruction.

A complete bibliography will be found in *Ziemssen's Cyclopædia*, vol. viii. p. 337; Nothnagel, *Specielle Pathologie und Therapie*, article "Geschwülste d. Peritoneum."

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## HYPERTROPHY AND STENOSIS OF THE PYLORUS IN INFANTS.\*

BY F. L. WACHENHEIM, M.D.,  
OF NEW YORK.

THE following addition to the sixty-odd hitherto recorded cases of hypertrophy and stenosis of the pylorus in infants has come under my observation:

Thomas M., aged five weeks, was seen by me for the first time on September 29, 1904. His mother stated that uncontrollable

\* Read before the Pediatric Section, New York Academy of Medicine, December 8, 1904.

vomiting had set in after the second week, although he had been exclusively breast-fed, the condition of the bowels meanwhile varying from constipation to moderate diarrhoea, with green stools. The family history was negative; her other child was quite normal. Examination of the infant revealed nothing except extreme loss of flesh and strength; abdominal palpation was rendered almost futile by the child's continuous crying. Dietetic experiments showed that albumin-water and ordinary barley-water were regularly vomited within twenty to thirty minutes, the curdled condition of the vomitus showing approximately normal acidity of the gastric juice. According to the mother's statement, the vomiting was forcible, not merely regurgitant; that it was not complete could be demonstrated with the stomach tube, whereby several ounces of fluid could be withdrawn from the stomach. Dilute barley-water and lime-water were usually, though not always, retained. After a week of observation I was led to suspect the presence of a so-called congenital hypertrophy and stenosis of the pylorus; a positive diagnosis was, however, unattainable, for neither a tumor nor gastric peristalsis could be made out. Lavage was resorted to, with some benefit; the vomiting had been, in a great measure, abated, when the infant, rather suddenly, went into fatal collapse on October 13th. On account of the extreme marasmus, the grave diagnostic doubts, and the disputed advisability of surgical intervention in these cases, operative measures had not been counselled; it turned out that in this case no other procedure could have been of the slightest use, and that its omission was an error, as I now freely admit, although the infant most probably would have succumbed to the shock of the operation.

A partial, but sufficient, autopsy was obtained with considerable difficulty, and performed within six hours, rigor mortis being still present. On opening the abdomen, the enlargement of the moderately congested liver and spleen attracted attention; the former organ completely overlapped the pyloric region, so that the almost cartilaginous mass of the pylorus could only be palpated by working deeply underneath; it was evident that it could not possibly have been made out during life. Not counting the pyloric end, the stomach had an extreme length of 10 cm., and was distended with air and a gelatinous fluid; the walls of the organ were tense and of about normal thickness, the folds of its pale mucous membrane almost obliterated. The pylorus was 3 cm. long, of remarkably firm consistency, projecting into the duodenum like a cervix uteri; its diameter of 14 mm. was in marked contrast to the diameter of only 8 mm. of the empty, flaccid, and somewhat congested duodenum. The lumen of the pylorus barely admitted a director 2 to 3 mm. in thickness; its walls had a thickness of 6 mm., whereof the greater portion evidently represented muscle. The mucous membrane appeared perfectly normal, and was thrown into heavy longitudinal

folds which must have rendered the already narrow orifice almost wholly impervious. The intestine was normal, save for a contraction and possibly deficient development of the lower ileum. The result of the autopsy was a positive diagnosis of hypertrophy and stenosis of the pylorus; the microscopic findings I shall give later on.

The first mention in literature of this disease dates from 1788, when Beardsley<sup>1</sup> published a case, whose status I shall discuss presently. Beardsley's report sank into oblivion, to be resuscitated at Osler's instance a year or two ago. In 1841 and 1842 Williamson<sup>2</sup> and Siemon-Dawosky<sup>3</sup> respectively published two cases that are typical, and will always remain classical. Then follows a great gap until 1888, when Hirschsprung<sup>6</sup> brought the subject before the profession once more, none of the intervening reports (Landerer,<sup>4</sup> Maier<sup>5</sup>) applying to infants, but giving cases in adult subjects only. It seems strange that so characteristic a lesion and so striking a clinical picture should have escaped observation for forty-six years; at any rate, no case came to autopsy, and we shall see that no case without operative or post-mortem autopsy can be accepted without reserve.

Since Hirschsprung's communication enough has been written about this disease to fill a good sized volume; a great part of this literature is, however, uncritical, and still more purely academic; verified reports are still scanty, even with the most liberal interpretation.

Clinically and pathologically, we may divide all the reported cases of congenital hypertrophy and stenosis of the pylorus into three groups.

1. There are those that attain an age beyond early infancy, present throughout their lives more or less symptoms of obstruction, in some cases even grow to maturity, and then seek operative relief. It is evident that here the stenosis must be of a moderate degree; the pyloric lumen, as a matter of fact, measures from 5 mm. upward.

2. We have to consider those infants that present for a few weeks similar symptoms, which, however, gradually yield to appropriate diet and medication.

3. Those babies that either are promptly relieved of an almost total obturation by surgical measures, or die within a few weeks of simple inanition.

The cases coming under the first head are fairly numerous; there is Beardsley's that died at the age of five years, those of Landerer and Maier, the second one of Hirschsprung, those of Henschel,<sup>8</sup> more recently those of Rosenheim (Sonnenburg),<sup>28</sup> Hansy,<sup>31</sup> and so on, latterly, that of Shaw.<sup>54</sup> Batten's<sup>30</sup> case is doubtful; it improved under treatment, and died at eleven weeks of bronchopneumonia. This group need not detain us further, for, even if now and then a

case, such as the last, may not admit of classification, these patients present no urgent symptoms in infancy, and therefore afford a different picture, both clinically and prognostically, from those to follow.

The second group is also quite well represented, and is of far greater interest. I shall refer to only a few reports, namely, those of Weill and Péhu,<sup>34</sup> Southworth,<sup>39</sup> Saunders,<sup>46</sup> Gardner,<sup>53</sup> Freund,<sup>55</sup> Variot,<sup>57</sup> and Stamm,<sup>66</sup> but could mention many more. We can discuss the status of this series to greater advantage in connection with the third group than by attempting to dispose of it separately, and shall therefore pass on at once to the latter. It is this, the type, which chiefly interests us, and will form the body of this paper; we have here the advantage of dealing with definite and tangible data which will form a convenient starting point. I present below a tabulated synopsis of the moderate number of cases that have come to autopsy, omitting the operated cases, which are probably more suitable to the paragraph on treatment, and have not always been carefully reported. A fitting introduction to this table is Williamson's classic account, which it will be worth while to quote in full:

"The infant, a male, died at the age of five weeks. At birth it was plump, and apparently healthy, but a few days afterward vomiting came on, and the matter ejected was coagulated milk. During the last fortnight the bowels were obstinately constipated, and the child seemed to be falling off considerably in flesh, until it gradually sunk exhausted. Upon dissection, the intestines were found collapsed and empty, and all the other visceral organs perfectly healthy, with the exception of the stomach, the pyloric extremity of which felt hard and indurated, forming a remarkable contrast to the soft and yielding parietes of that viscus when emptied of its contents. Upon removing the stomach it was found that the pyloric orifice was so contracted as scarcely to admit a small silver probe, a state which might perhaps in part account for its being nearly filled with coagulated milk. Upon slitting open the pyloric orifice, it was evident that the tissues entering into the composition of the parietes of the stomach had greatly lost their normal appearance.

The mucous coat was slightly thickened, while scarcely a distinct remnant of the middle or muscular tunic was observable. On the other hand, the submucous cellular tissue was so much hypertrophied and indurated as seemingly to be the only tissue contained between the mucous and peritoneal coats."

Williamson's histological diagnosis of "scirrhus" cannot, of course, be accepted; otherwise his description is perfect. We should not even criticise the "scirrhus" too severely; many of us still speak of uterine "fibroids."

We may now pass on to our table:



No.	Author.	Sex.	Age at onset.	Age at death.	Bowels.	Tumor felt?	Dilatation		Lumen of pylorus.
							or peristalsis in vivo	p.m.	
1	Williamson, <sup>2</sup>	M.	3 dys.	5 wks.	Constipation.	No	No	?	2 mm.
2	Dawosky, <sup>3</sup>	?	4 wks.	10 wks.	"	"	"	?	3 mm.?
3	Hirschsprung, <sup>6</sup>	F.	10 dys.	4 wks.	"	"	"	No	2-3 mm.
4	Peden, <sup>7</sup>	?	3 dys.	12 wks.	"	"	"	"	5 mm.
5	Pitt, <sup>9</sup>	?	3 wks.	7 wks.	?	"	"	"	?
6	Finkelstein, <sup>10</sup>	F.	at birth	13 wks.	Constipation.	Yes	Yes	Yes	?
7	Gran, <sup>11</sup>	F.	2 wks.	16 wks.	Diarrhœa.	No	"	"	3 mm.
8	DeBruyn Kops, <sup>12</sup>	M.	at birth	7 wks.	Constipation.	"	No	"	5 mm.?
9	Thomson, <sup>13</sup>	M.	10 dys.	4 wks.	Moderate constipation.	"	"	"	5 mm.?
10	Thomson,	M.	4 wks.	10 wks.	Constipation.	"	"	"	1 mm.?
11	Thomson, <sup>14</sup>	F.	1 wk.	7 wks.	?	Yes	"	No	?
12	Schwyzer, <sup>15</sup>	F.	2 wks.	11 wks.	Constipation and diarrhœa.	No	"	Yes	2 mm.
13	Schwyzer, <sup>16</sup>	M.	?	7 wks.	Constipation.	"	"	"	2 mm.
14	Ashby, <sup>17</sup>	?	1 wk.	7 wks.	"	"	"	"	2-3 mm.
15	Rolleston and Hayne, <sup>23</sup>	M.	at birth	8 wks.	"	"	"	"	2 mm.
16	Still, <sup>25</sup>	M.	6 wks.	12 wks.	Diarrhœa.	Yes	"	slight	3.5 mm.
17	Still,	M.	6 wks.	14 wks.	Constipation.	"	Yes	Yes	3.5 mm.
18	Still,	M.	3 wks.	14 wks.	"	"	"	"	3.5 mm.
19	Cautley, <sup>26</sup>	M.	5 wks.	14 wks.	"	No	No	?	2 mm.
20	Cautley,	M.	at birth	8 wks.	?	"	"	No	closed.
21	Pritchard, <sup>32</sup>	M.	3 wks.	9 wks.	Constipation.	"	Yes	Yes	3 mm.
22	Cautley, <sup>33</sup>	F.	at birth	12 wks.	Constipation and diarrhœa.	"	No	"	2 mm.
23	Rolleston and Crofton-Atkins <sup>35</sup>	M.	2 wks.	8 wks.	Constipation and diarrhœa.	"	"	"	1-2 mm.
24	Blackadder, <sup>42</sup>	M.	2 wks.	10 wks.	Constipation.	"	"	"	?
25	Cautley, <sup>43</sup>	?	?	8 wks.	?	?	?	"	1-2 mm.
26	Saunders, <sup>46</sup>	F.	2 wks.	16 wks.	Diarrhœa.	Yes	Yes	"	2-3 mm.
27	Nordgren, <sup>47</sup>	F.	at birth	11 wks.	Constipation.	No	No	No	4 mm.
28	Nordgren,	M.	3 wks.	7 wks.	"	"	"	Yes	5 mm.
29	Riviere, <sup>52</sup>	M.	2 wks.	8 wks.	Constipation and diarrhœa.	"	"	No	?
30	Freund, <sup>55</sup>	M.	?	9 wks.	?	?	?	?	?
31	West, <sup>56</sup>	M.	3 dys.	5 wks.	Constipation and diarrhœa.	Yes	Yes	Yes	?
32	Cautley, <sup>62</sup>	M.	3 wks.	14 wks.	Constipation and diarrhœa.	"	"	"	1-2 mm.
33	Cleveland, <sup>63</sup>	M.	2 wks.	12 wks.	Constipation.	No	"	"	5 mm.
34	Dorning, <sup>65</sup>	M.	at birth	11 wks.	Constipation and diarrhœa.	Yes	No	slight	2 mm.
35	Wachenheim,	M.	2 wks.	7 wks.	Constipation and diarrhœa.	No	"	slight	2-3 mm.

A few explanatory words may be added. The vomitus was usually acid; free HCl was found in a few cases, bile in Nos. 13 and 26. In many cases the palpated tumor was almost certainly not the pylorus, but the tensely distended fundus. The lumen is often reported as admitting "a fine probe," "a No. 6 catheter," "the blade of a pair of forceps," and so on. I have endeavored, for the sake of easy tabulation, to reduce all such statements to millimetres.

The average age at onset is two weeks; at death nine weeks and a half. In view of the remarkable uniformity of the above statistics, we may safely regard every case that survives beyond four months as outside of this clinical group. Indeed, it stands to reason that an almost or quite complete occlusion of the gastrointestinal aperture is incompatible with longer life.

Males predominate in the ratio of 2.5 to 1. Most of the infants were breast-fed; improper food played no causative part. The

intensity and frequency of vomiting were directly proportional to the quantity and consistency of the ingesta, as happened in my case. The acidity often noted in the vomited matter was probably not often due to free HCl, but in most cases this point was not determined. Biliary vomiting occurred a few times; it seems inconsistent with the anatomical conditions, and might give rise to diagnostic doubts, as in Schwyzer's second case. Uncertainty is also bound to arise when diarrhoea and green stools are present, especially during the warmer months. It requires a week or so of observation to clear away doubts in all but the typical cases, and often the diagnosis will not advance beyond probability. For my part, I would venture farther, and assert that most cases remain unrecognized and unreported, being passed by as mere gastrointestinal catarrhs, and I am supported in this opinion by such authorities as Cautley.

The palpation of the pylorus, as suggested above, is an uncertain quantity, and is frequently rendered difficult or impossible by the almost constant crying of the infant, with resultant tension of the abdominal parietes. Opinions vary widely as to the presence or absence of pain; while the crying may in part be due to hunger, the violent contractions of the gastric muscle, as sometimes evinced by visible peristalsis, and the forcible vomiting must cause great distress. Peristalsis and dilatation were visible usually only when the stomach was well filled, and sometimes only in the terminal stages of the disease, in many cases not at all. This appears quite natural, since the recorded post-mortem measurements of the stomach rarely show more than moderate dilatation, the extreme length rarely equalling 12 and often not exceeding 9 cm., and the walls of the viscus being but very slightly changed, if we except the pyloric end.

In view of the usual off-hand designation of this affection as congenital, it is curious that most cases show no symptoms during the first week or two, sometimes even up to six weeks, the onset being in general quite abrupt. This point is most perplexing and not readily explainable; we should infer from this circumstance alone that the question of pathogenesis is difficult to answer; as a matter of fact, clinicians have been, for some time, grouped into three factions, two holding opinions diametrically opposed, while the third occupies a middle position.

Dating from Thomson's reports, many cases have been recorded as "congenital spasm of the pylorus," often such as have not come to autopsy or have apparently recovered; some, however, like those of Thomson himself, of the true Williamson type. Still,<sup>24</sup> whose anatomical studies are invaluable, is convinced that the chief element in this disease is spasm, that the hypertrophy is secondary and not of a high degree, the relatively short duration of the affection admitting of only moderate muscular overgrowth, that serious and

permanent changes are inconsistent with the reported cures, and that the narrowing of the pyloric lumen, as found post-mortem, is often very moderate. Still's own cases, given in the above list, are, unfortunately, not among the most typical; the lumen in these cases was indeed "3.5 mm. or more." The onset was unusually late, and the duration of life beyond the average; in fact, they form the transition, if one exists, to cases such as Batten's, which we have been compelled to exclude from consideration here. Pfaundler,<sup>10</sup> writing shortly before Still, goes farther; he claims that the pylorus of an entirely normal stomach may remain contracted post-mortem, thus assuming the consistency of an annular tumor with apparently hyperplastic walls, narrowing the lumen almost to obliteration; secondly, he insists that the anatomical and histological pictures, presented by Hirschsprung and others as pyloric stenosis, agree perfectly with the aforesaid systolic stomach; thirdly, he instances the reported recoveries from similar symptoms, refers to our ignorance of any anatomical basis for this affection, and concludes that we are dealing with a functional spasm alone. Schmidt,<sup>44</sup> in connection with his operated case, to be noted farther on, agrees entirely with Pfaundler; his case is, however, a more than doubtful one, the lumen of the pylorus measuring over 5 mm. Freund<sup>55</sup> goes a step farther; asserting that the spasm is probably neuropathic, and associated with or even caused by hyperchlorhydria. Hyperchlorhydria in infants had recently been discovered by Knöpfelmacher,<sup>45</sup> and from our knowledge of certain spasms in the adult Freund's view might appear plausible, but for the fact that free HCl was not always present in the vomited matter; even so, free HCl without quantitative data does not imply hyperchlorhydria by any means.

I have gone into the spastogenic theory somewhat deeply, because it does not represent the prevailing opinion. Stern,<sup>20</sup> the first to operate for this condition, considers it almost wholly an anatomical lesion; his article being the occasion for the just quoted statement of Pfaundler. Meltzer,<sup>21</sup> whose case was the second to be operated upon, makes a strong plea, from the standpoint of the pathological anatomist, for the hypertrophic (hyperplastic) theory; he insists that a spasm, lasting a few weeks only, cannot cause the excessive muscular development found in these cases, and that the concomitant increase of the submucous connective tissue shows hyperplasia and not merely compensatory hypertrophy; in the severe cases, that will hardly admit of the passage of a probe, pyloric spasm can contribute but little to a condition already intolerable. Cautley and Dent,<sup>50</sup> the former of whom has seen one-eighth and reported one-fourth of all recorded cases, take the same position; the remarkable uniformity of Cautley's unique experience must be allowed to have especial weight. A strong point in favor of the observers of the second group is, that their stand is not incompatible with a compromise in the direction of the following.

We thus pass on, quite naturally, to the third group, who are prepared to accept both propositions. They believe, and I feel compelled to agree with them, that there is one condition that consists in an overgrowth of the muscular and submucous coats of the pylorus, narrowing the orifice of that viscus, and aggravated by a tonic contraction which is in all probability due to the abnormal innervation that usually accompanies muscular hypertrophy. They also admit a second condition, a pyloric spasm pure and simple, resting possibly on the hypothesis of Freund, and associated with some slight secondary muscular hyperplasia. It is evident that the prognosis of the former lesion is bad, and of the latter fairly good. Finally, we must reckon with the possible occurrence of intermediate or transitional states. The evidence on this point is incomplete, but it certainly is curious that cases like Still's<sup>25</sup> and Nordgren's,<sup>47</sup> with moderate stenosis, have a pyloric wall only about 4 mm. in diameter; while severe cases, such as Schwyzer's,<sup>16</sup> Cautley's,<sup>51</sup> and mine, have a pyloric wall of far greater thickness. While, from the clinical aspect, this matter must remain, for the time being, academic, it may, eventually, have important and interesting pathological bearings. Clinically, we can only consider two distinct affections, whose symptoms are almost precisely alike, but whose anatomy, course, and prognosis differ very widely.

Schotten,<sup>61</sup> in his recent excellent monograph, plainly accepts this view. When he says that the prognosis of hypertrophic stenosis is hopeless, he clearly considers all reported cures to apply to cases of simple spasm; in other words, he assumes the existence of two distinct diseases. This does not, of course, imply that all cases of pyloric spasm recover, but from the scarcity of autopsies, at most a small minority of those in our table, a fatal result must be unusual.

Whether the pyloric abnormality is a deformity or a hyperplasia in the sense of a new-growth cannot be decided. There is some evidence in the former direction. Ashby's second case, excluded from my table, was an infant a few days old, that died after an operation for atresia of the anus; the pyloric orifice was found to be quite impervious, the organ itself much thickened. Two similar cases are reported by Hammer;<sup>27</sup> related to these are several records of congenital occlusion of the duodenum. I cannot determine whether or not these facts apply here; the question seems to me an open one. As to the theory of a new-growth, it has so far nothing to sustain it, yet need not be absolutely rejected on that account, since the whole subject of benign and other new-growths is still shrouded in mystery. We know of no strictly analogous lesion in any other organ.

Let us pass on to anatomical details, prefacing them with a few remarks concerning the not generally known normal conditions. Still<sup>25</sup> and Pfaundler<sup>18</sup> have made valuable contributions to our knowledge of the dimensions of the normal infantile pylorus, which

it will repay to give here in condensed form. Still's results are not very precise, though very probably quite correct; he states the average total thickness of the pyloric wall at 2.5 mm. in infants of about six months, with an extreme range of about a third more or less; the minimum for the normal lumen he sets at 4 mm., a rather low and conservative estimate. Pfaundler gives us detailed measurements of the pyloric orifice, 6.3 mm. at birth, 7.3 mm. at two months, 8.5 mm. at six months, and 10.5 mm. at twelve months, all averages, of course. According to both authorities, a lumen of over 5 mm. at two or three months, as frequently recorded in our tables, can hardly amount to a serious anatomical lesion, as should, indeed, be obvious without much investigation; the importance of this point will be emphasized in discussing treatment. Still's measurements seem to settle conclusively that a pyloric wall over 4 mm. thick is pathological. So far, all is clear.

When the orifice of the organ measures less than 3 mm., the attendant spasm of the hypertrophied muscle seems sufficient to cause almost complete and permanent closure; that this is, however, not quite total, is shown by the passage of thin fluids, occasional biliary vomiting, and by the almost invariable presence of fecal matter in the bowel, sometimes even a diarrhoeal condition. Freund made some interesting pressure experiments, showing the resistance of the pyloric sphincter to abnormally high hydrostatic pressure, not a drop passing through; this circumstance had been somewhat cursorily noted by a number of previous observers. It seems that these results depend in part on post-mortem rigidity, in part on valve action of the marked folds of the mucous membrane; the valve action would, naturally, increase with abnormal hydrostatic pressure, yet might not exist to the same degree during life. That this aspect of the case has some merit is shown by the clinical fact that vomiting is far more apt to follow a full meal than teaspoonful doses of thin fluids, also by the undoubted temporary relief afforded by the stomach tube.

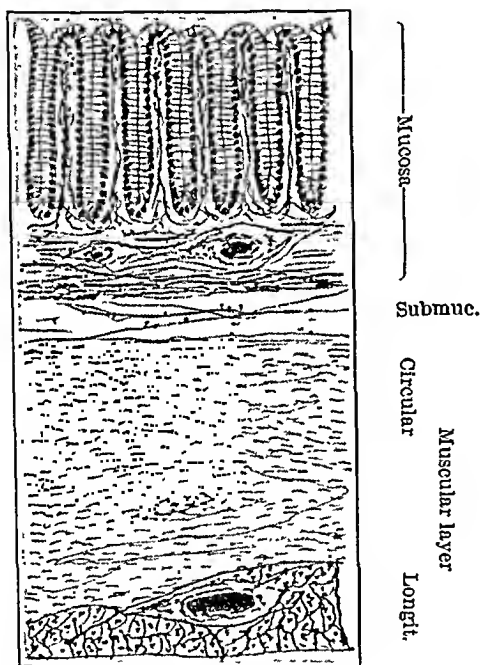
I proceed to the histological findings in this disease, beginning with a study of my own case, and comparing this with the, save for a gastritis, normal stomach of an infant of the same age. For the latter specimen I am indebted to the kindness of Dr. S. V. Haas.

In the mucosa and its glands there is nothing abnormal. The submucosa is of about twice the normal thickness, with considerable round-cell infiltration. The muscular coats are enormously hypertrophied; the circular coat has four to five times the normal thickness, and the overgrowth of the longitudinal muscle is proportionately nearly as great. In the muscular coats (chiefly in the circular) there is also a moderate amount of inflammatory reaction, but, perhaps, not more than one would expect with so enormous a hypertrophy in infantile tissue. There is no change in the bloodvessels out of proportion to the excessive development of the other tissues.

The accompanying illustrations will fully illustrate the disturbed relations and measurements of the various parts in my case. Both sections are taken from the thickest portion of the viscus.

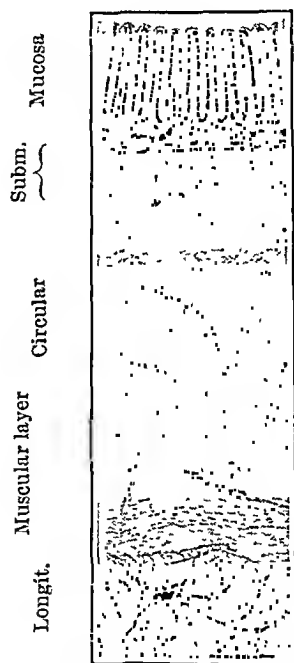
It is interesting to compare the findings of Finkelstein,<sup>10</sup> who claims that the hypertrophy is chiefly in the longitudinal coat. Most other observers have laid stress on the increase of the circular coat; this seems to be a smaller error in the opposite direction. The hypertrophy of both layers in my case is so evident that it must be considered the usual picture. Upon reflection, we readily see that it could not be otherwise; to overcome the abnormally firm closure of the pylorus by the circular layer, there must be a compensatory hypertrophy of the longitudinal coat, whose function is

FIG. 1.



Normal pylorus at seven weeks (cross-section).  $\times 25$ .

FIG. 2.



Case of Thomas M. Pylorus (cross-section).  $\times 12\frac{1}{2}$ .

that of dilatation and propulsion. The hyperplasia will naturally be somewhat greater in the circular layer, where it is primary. In accordance with this is the more abundant evidence of interstitial inflammation in the circular layer, where we are dealing with the primary hyperplasia; in the at least partly compensatory overgrowth of the outer coat, round-cell infiltration is not so marked.

The theory of spasm cannot, of course, apply to such a case as this at all. Aside from the very plainly visible new-growth of tissue, the thickening of the longitudinal coat does not fit into such an hypothesis. It hardly seems worth while to go into this matter

deeply, for the bulk of the pylorus in my case is at least three times as great as normal, and the defender of the spastic theory can be at once confronted with the demand that he account for the presence of the redundant two-thirds of tissue. If the thickening of the pylorus were due to spasm the organ would be shortened, its total volume remaining unchanged; in my case the length as well as the diameter of the pylorus is increased, as can be seen by its cervix-like projection into the duodenum.

The rarity of the disease has undoubtedly been exaggerated. When a single English observer can furnish a long series of cases, the failure of French authors to produce a single one is explainable in only one way. The very peculiar distribution of the available records convinces me that hundreds of cases have been overlooked within the last ten years. With an obscure disease this would not cause astonishment; in view of the exceedingly simple anatomical picture here presented it is most remarkable. We have every reason to expect an enormous increase of material within a brief period.

The diagnosis, in many cases, is not easy; in summer the possible combination of pyloric stricture with a digestive disturbance will almost always prove puzzling, especially as, among the poorer classes, the histories given by the mothers are unreliable. I have only to mention the fact that in my service the anamnesis of diarrhœa is rarely volunteered, but has to be elicited by leading questions; we all recognize the overpowering tendency to answer leading questions in the affirmative. The key-note in this affection is the combination of obstinate vomiting, equally obstinate constipation, and gradual loss of weight; an important point in the vomiting is its violence and close dependence on the ingestion of food, the quality of which is almost immaterial; meanwhile the appetite, as might be expected, is ravenous; this complex of symptoms is highly characteristic. I have referred sufficiently to such matters as visible dilatation and peristalsis, the doubtful palpability of the pyloric tumor, the normal condition of the peptic function as revealed by the stomach tube, and need not weary you with a repetition of these data.

Diagnosis is but the preliminary step to prognosis; while the academic discussion of the latter is easy, the problem in the individual case becomes almost unsolvable. If Pfaundler's opinion is correct, most cases should recover. I have sufficiently stated my reasons for excluding all cases of mere pyloric spasm from this discussion; in the cases of true stenosis, the outlook is for a rapidly fatal issue. The only demand on the diagnostician, therefore, is to establish an anatomical obstruction; this has hitherto been feasible only by prolonged observation and *ex juvantibus*, whereby the opportunity for relieving the patient is apt to be lost by undue delay. Thus, the clinician's task is trying and embarrassing; time

is required for study, yet a true stenosis of the pylorus in a young infant does not permit much temporizing.

As it is impossible, in a particular case, to determine at once whether mere spasm or organic obstruction is playing the chief role; and since operative intervention, as we shall see, entails a high proportionate mortality, it would appear in order to begin by assuming the presence of the milder condition, from which recovery is the rule, and treat the patient accordingly. In this connection Freund's method is of great interest, as it resulted in a permanent cure of one-third of his cases, while another third died only in consequence of intercurrent affections after apparent cure. His treatment consists in giving Carlsbad (Mühlbrunnen) water in addition to the usual diet—*i. e.*, breast-milk, later on whole milk, resorting to surgery only when this treatment fails. Although his procedure rests on the above-mentioned theory of spasm from hyperchlorhydria, which he acknowledges to be often absent, yet his results warrant further trial. Some benefit also seems to be derived from lavage; at least, it diminishes the strain on the infant organism, caused by frequent and violent spells of vomiting. I would also refer to the advantage of giving small and frequent meals of highly diluted albumin-water and barley-water; this plan naturally failed in my case of extreme stricture; in spastic cases it should prove vastly beneficial, if resorted to before grave exhaustion has supervened.

The procedures mentioned embrace about all that can be recommended in the way of medical measures, and I consider it an error to continue them beyond two weeks, unless the infant begins to gain in strength and especially in weight, which latter should be carefully controlled. Further than this, all treatment must be strictly surgical, as affording the only chance, though not a very brilliant one.

I shall begin the consideration of the surgery of this disease by once more giving all available reports in tabular form:



No.	Author.	Age.	Operation.	Result.	Lumen of pylorus.
1	Stern, <sup>20</sup>	6 weeks.	Gastroenterostomy.	Fatal in 12 hrs.	2 mm.
2	Meltzer (Meyer), <sup>21</sup>	6 "	Gastroenterostomy (Murphy button).	" 30 "	1-2 mm.
3	Meyer (Adier), <sup>22</sup>	11 "	Gastroenterostomy.	" 16 "	2-3 mm.
4	Abel (Kehr), <sup>23</sup>	8 "	"	Cured.	2-3 mm.
5	Löbker, <sup>27</sup>	11 "	"	"	?
6	"	7 "	"	Fatal.	?
7	Kehr, <sup>26</sup>	8 "	"	Cured.	?
8	Fritsche, <sup>33</sup>	?	"	"	?
9	Lange (Braun), <sup>40</sup>	10 weeks.	Pyloroplasty.	Fatal.	1-2 mm.
10	Nicoll, <sup>41</sup>	6 "	Divulsion.	Cured.	?
11	Schmidt, <sup>44</sup>	8 "	"	"	5-6 mm.
12	Cautley and Dent, <sup>50</sup>	8 "	Pyloroplasty.	Cured; died 13 weeks after of intestinal disorder.	?
13	" " "	6 "	"	Cured.	?
14	Burghard, <sup>51</sup>	8 "	Divulsion.	"	?
15	Murray, <sup>51</sup>	18 "	Pyloroplasty.	"	?
16	Stiles, <sup>51</sup>	9 "	Pylorotomy.	Fatal.	?
17	"	5 "	Gastroenterostomy.	"	?
18	"	7 "	Divulsion.	Cured.	?
19	"	4 "	"	Fatal.	?
20	"	11 "	"	Cured.	?
21	Graanboom, <sup>48</sup>	3 "	Pyloroplasty.	Died 6 wks. later from inanition.	2 mm.
22	Trantenroth, <sup>49</sup>	7 "	Gastroenterostomy.	Cured.	2-3 mm.
23	Freund, <sup>53</sup>	10 "	"	Died 19 weeks later from intestinal hemorrhage.	?
24	Greeff, <sup>58</sup>	?	"	Fatal.	?
25	Gallant, <sup>59</sup>	5 weeks.	"	Fatal in 6 hrs.	2 mm.
26	Mackay, <sup>60</sup>	20 "	"	" 36 "	3 mm.
27	"	6 "	Divulsion.	" 22 "	?
28	Schotten, <sup>61</sup>	5 "	Gastroenterostomy.	Cured.	?
29	"	6 "	"	Fatal in 20 hrs.	?
30	"	20 "	Gastroenterostomy (uncompleted).	Fatal.	3 mm.
31	McCaw and Campbell, <sup>64</sup>	?	Pyloroplasty.	Fatal in 6 days.	8 mm.!
32	Grisson, <sup>67</sup>	9 weeks.	Divulsion.	Cured.	2 mm.

(Cases 14 to 20 reported very briefly by Cautley and Dent.)

## SUMMARY.

Operation.	Cured.	Fatal.	Total.	Mortality.
Gastroenterostomy (suture) . . . . .	6	10	16	62 per cent.
" (Murphy) . . . . .	0	1	1	100 "
Pylorotomy . . . . .	0	1	1	100 "
Pyloroplasty . . . . .	3	3	6	50 "
Divulsion . . . . .	6	2	8	25 "
Total . . . . .	15	17	32	53 "

This summary, which gives a highly favorable result for divulsion, is in great need of correction for inaccuracy. Thus Schmidt's case is probably not one of true stenosis, and might have recovered without operation; in Case No. 31 the operation seems to have been positively harmful, but in view of the before-stated diagnostic difficulties, the surgeon is in every way excusable; cases 14 to 20, mere private communications to Cautley, and published without comment, are too briefly reported to be worthy of inclusion. Omitting these 9 cases, our summary is as follows:

Operation.	Cured.	Fatal.	Total.	Mortality.
Gastroenterostomy (suture) . .	6	9	15	60 per cent.
“ (Murphy) . . . . .	0	1	1	100 “
Pyloroplasty . . . . .	2	2	4	50 “
Divulsion . . . . .	2	1	3	33 “
Total . . . . .	10	13	23	57 “

Even these figures are probably too favorable; in many more cases, as shown in the table, the pyloric lumen is not reported; some of these may be merely cases of spasm. Of the 11 positive cases, 8 died, 73 per cent.; this is probably near the true proportion, for in this series, as in all surgical ones, many unfortunate cases never appear in print, while successful ones rarely escape notice. I may mention that Freund's case seems to have died from the tearing out of a suture; the result is therefore reckoned among the failures.

The summary, given above, seems to show about equally good results for all procedures, except the Murphy button method, which has not had a fair trial. Dr. Willy Meyer has kindly favored me with a communication concerning his case, in which the Murphy button was used; the button employed was far too large, and he has had no opportunity to employ the small ones he has ordered for a possible future occasion; he is not, however, inclined to regard that method very favorably. Not being a surgeon, I forbear descanting on the relative merits of the other methods; moreover, the question is still open, and can be settled only by further trials. It will be noted that German surgeons favor gastroenterostomy, the other methods being preferred in England. As to divulsion, the fatal cases seem on autopsy to show a rapid recurrence of the stenosis, leading one to suspect that the cures embraced mostly spastic cases without serious organic obstruction.

I feel that, in spite of every effort to give a painstaking and exhaustive analysis of the subject of hypertrophy and stenosis of the pylorus in infants, the general impression is one of uncertainty, and in many points quite confused. I also feel, much to my regret, that this impression is only too fully warranted by even a careful summary and intelligent discussion of the facts in our possession.

ADDENDUM. Shortly after the above was written there appeared a monograph by Ibrahim (*Die angeborene Pylorusstenose im Säuglingsalter*, Berlin, 1905), in which he reports 7 cases, 4 of which recovered, 1 died at eleven months, and 2 were unsuccessfully operated upon (gastroenterostomy) at eight and ten weeks respectively. Ibrahim obtained a complete autopsy of one of these; the lumen of the pylorus was 4 mm., and the hypertrophy affected almost wholly the circular layer, which had 2.3 times the normal thickness; the case thus resembled those of Still. Ibrahim proposes a new theory, namely, that there is an anatomical stenosis in early infancy, which undergoes spontaneous cure by compensatory hyper-

trophy in most cases; these cured cases cannot therefore be referred to simple spasm. Observe, however, the differences from such cases as those of Cautley and myself: first, the much wider, in fact, almost adequate, lumen; second, the almost total absence of hypertrophy in the longitudinal muscularis. Ibrahim's case is assuredly not typical. His theory is, however, worth mentioning, even if it rests, so far as our knowledge goes, on anatomical premises which have not been demonstrated and may be without foundation. It seems far-fetched to treat of this affection as a quasi-normal process; on the other hand, the possibility of a spontaneous cure of very moderate degrees of muscular hypertrophy cannot be rejected finally, as matters now stand.

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## A CASE OF DERMOID OF THE FEMALE URINARY BLADDER.

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Miss H., Kansas, aged eighteen years, first consulted me in September, 1904. A brunette, rather slender and somewhat frail in appearance. Very nervous and emotional, indicating previous suffering. Without any history of definite antecedent ailments, though claiming to have always been delicate. Nothing noteworthy in the family history bearing on her present condition. Some five years since she began to observe a painless urinary frequency. It was both diurnal and nocturnal and continued, varying in intensity, until one year ago, when dysuria became a prominent symptom. From that time until she came under observation periods of intense suffering, irregular as to time and duration, were noted. After a paroxysm of cystospasm and tenesmus, relief followed the expulsion of a small calculus. Neither at these periods, nor during the intervals, was there any hæmaturia. As near as could be learned, these extrusions averaged a semi-monthly repetition. The calculi were not voided into the vessel with the urinary stream, but it was alleged that they were always removed from the vulva by the patient.

A considerable number of these concretions were preserved by the patient and presented for identification at the first consultation. The smallest weighed 5 cgm.; the largest 5 decgm. Their basic shape was pyriform, at times resembling a club; quite a number of them preserving this basic form were curved, approaching a comma, and at times an interrogation point in contour. Occasionally they described a sigmoid.

From the apex of most, if not all, there protruded a hair with a terminal investing root sheath. The color of the hirsute nucleus was that of those upon the bearer's head and mons.

The urine was large in quantity and low in gravity, with an abundance of pus cells in the sediment. The latter were the only adventitious elements worthy of remark.

The patient was very sensitive and hyperæsthetic, yet under local anæsthesia a cystoscopy became possible. In passing, it may be observed that the provisional diagnosis of dermoid was suggested. A most tenable objection to this view was that of hysterical introduction. This was entertained, but rejected. Though recognizing the urinary bladder as a favored receptacle among these neurotics, in this instance, at least, we were able to dismiss this from consideration, for reasons to appear later on.

The cystoscope revealed a congested and chronically inflamed mucosa, and lying in the trigone was a good-sized stone, weighing 19 gm. It was irregularly spherical; beyond and above this three smaller calculi, approximating the forms already described, and each containing a hair, about which clustered the slender concretions, were readily discernible. The calculi were phosphatic in composition. Since the largest was not subjected to cleavage, the character of its nucleus remains uncertain.

Beyond and to the right of the right posterior angle of the trigone, seemingly some distance from the right ureteral ostium, a projection from the mucosa indicated the presence of a tumor. Its exact size, color, form, and relations could not be noted at the time, owing to a vesical intolerance spastically crowding the instrument.

The patient being prepared in the usual manner, a general anæsthesia was administered. Thoroughly dilating the urethra, an effort was made to drag the stone through the expanded canal. This proving practically impossible without running the risk of a subsequent incontinence, and not wishing to crush the specimen, the suprapubic route was substituted.

Removing the calculi, the dermoid was located and with some difficulty seized, brought into view, and excised. It proved to be no larger than the half of a very small raspberry. Its mucous aspect resembled the former, both to the touch and in appearance. Under the loop some seven or eight protruding hairs were visible; indeed, if viewed in a proper light, they could be readily seen by the unaided eye.

The patient made an uneventful recovery. Cystoscopy, done at leisure and without local anæsthesia prior to her dismissal, disclosed the bladder with a minimum of hyperæmia. The former seat of the fetal inclusion was plainly visible; a very small, stumpy, circular disk marked its former site.

Sections of the "growth" were made by Prof. Frank J. Hall, pathologist to the Kansas City Medical College, a description of which is herewith appended.

Judging from the scant literature on the subject of dermoids in this locality, they may be regarded as among the surgical curiosities, and yet, in view of all the available data in this case, diagnosis was easy, even without the aid of instruments of precision.

It is evident that until adolescence the presence of an ectodermic alien might remain unresented. As development proceeds, however, the growth and shedding of the hairs would soon usher in a disturbance. The history of our case proves this assumption corroborative.

As the hairs grew and projected into the urinary reservoir, calcareous deposition from its excrementitious contents must have been greatest upon their distal ends. The latter being exposed longest, one can readily apprehend the tendency to club forms. For the same reason, owing to increasing and increased weight, the peculiar curvings described were quite natural. Again, the root sheath always presenting at the apex and thinnest portion of the calculus, plainly indicated a short exposure to the decomposing urine. The stone evidently fell and escaped as soon as it reached maturity.

The apical root sheath negated the always plausible theory of hysterical perversion. In the latter event, more than likely, the deposition would have proceeded in a regular manner, forming ovals or spheres, and, if retained for some time, facets, the result of attrition, would have been present.

However frequent these fetal inclusions or rests may be in other parts of the body, they are certainly very rare in the urinary bladder.

Quite a number of recorded instances occurring in the neighborhood of the ureteral opening contained, among other elements, muscle and cartilage cells, as well as sarcoma cells. These rather suggested the character of a neoplasm, and from their nature and location probably originated in the Wolffian body.

Since hæmaturia at some time in the history of a vesical neoplasm is among the most characteristic, if not most prominent symptoms, its absence in our case was exceedingly noteworthy. It was doubly so after the cystoscope revealed the presence of a tumor. In the face of both the positive and negative testimony, it would have been impossible to escape the conclusion that this must be a dermoid.

Suppurating dermoidal evacuations by the vesical route are not uncommon. This is an entirely different matter and cannot be classed with the subject under discussion.

We are all aware that a small percentage of vesical calculi is subject to relapse after removal. The usual causes are well understood. Is it not possible that this may be an occasional factor, some element in the ectodermic tissue forming a nucleus for a renewal of the concretion?

Technically, no doubt, the entire operative procedure was feasible *via* the urethra. But whether the valuable specimen forming the basis of this contribution could have been secured intact is not so certain.

#### DR. HALL'S REPORT.

The following description of the bladder "tumor" presented September 15, 1904, for microscopic examination is respectfully submitted:

*Gross Description.* The tumor is shaped like a sphere vertically depressed. In horizontal direction the tumor measures 8 mm.; in vertical, 5 mm. It presents at the point of attachment to the bladder a small, fibrous pedicle about 1 mm. in diameter.

The color of the tumor is light pink, and in consistence elastic and soft. The surface is marked by many small dimples and rugosities. Under low magnification, or even naked-eye inspection, one makes out, emerging from the dimpled spots on the surface, rather fine hairs. One of these had a considerable deposit of urinary salts about its free end.

*Microscopic Description.* Sections were cut vertical to the great diameter of the tumor. Under low power the growth presents a covering of squamous epithelium resting upon typical dermal structures.

The covering epidermis shows a well-developed stratum granulosum and lucidum. The interpapillary plugs of epithelium are rather irregular in both size, shape, and distribution, but otherwise normal.

Connecting with the surface are several deep and irregular depressions lined with epidermis, and receiving at their bottoms the orifices of sebaceous glands and hair follicles. The sebaceous glands are large and typically formed. Here and there in the section are presented variously cut hair follicles and sebaceous structures.

Deeply situated in the section are several fairly large aggregations of cells which present, on close examination, the structure of glandular epithelium. The basal row of cells in these masses are tall, columnar, narrow at the free ends, and somewhat ragged. The nuclei are round and vesicular and placed near the bottom or base of cell. The cell cytoplasm stains very lightly with eosin and seems to be filled with clear, spherical spaces, which I believe to be the cavities left from absorption of fat by ether in the preparation of the sections. In other sections, typical areas of tubular glands present in variously cut sections. Here the epithelium is tall, columnar, and

presents the features distinctive of the axillary sweat glands. In the close neighborhood of these glands are many irregular spaces lined with double layers of pavement epithelium. The lumina of these spaces contain an unstained granular matter, evidently coagulated secretion. At a few points these irregular channels can be traced to the masses of gland tubules, and are evidently very tortuous and dilated ducts.

The connective tissue throughout the growth is disposed similar to that of the normal corium and constructed of the same elements. The growth is well supplied with veins and arteries whose walls are apparently somewhat thicker than vessels of corresponding size in the normal corium. In the papillary portion of this corium are areas of round cells. Here is noted frequent nuclear degeneration; the nuclei being drawn out into various bizarre threads and clumps of intensely staining chromatin.

Withal the growth is a typical dermoid.

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## TWO CASES OF ULCERATIVE PERFORATION OF THE RECTUM ORIGINATING FROM A GONORRHEAL SALPINGITIS.

BY JOSEF OTRADOVEC, M.D.,  
OF CHICAGO.

(From Prof. Chiari's Pathological-Anatomical Institute, Prag.)

THE ordinary conception of the pathological anatomy of gonorrhœa is that it is a superficial process confined mainly to mucous membranes. But the gonococcus is sometimes capable of penetrating tissues and there producing abscesses and even ulceration. Of especial note is the research of Wertheim,<sup>1</sup> who showed the gonococcus to be present not only in the pus, but also in the tissues of a pyosalpinx. Wertheim found, by using the staining method of Kühne (carbolic-methylene blue), or even by staining with a simple methylene-blue solution, absolutely characteristic gonococci, not only in the epithelium, but also localized in the uppermost layers of the connective tissue, far more often lying in the cells than in the intercellular substance.

Thus, also, Frisch<sup>2</sup> found, in examination of microscopic sections of a rectal mucosa, pieces of which were extirpated both during life and after death, that in places the cylinder epithelium and partly the rectal mucosa itself, with the superficial portion of the crypts of Lieberkühn, were wanting, so that even macroscopically distinctly visible ulcers were seen. In the crypts, as well as in the connective-tissue spaces between the crypts and in the partly infiltrated mucosal connective tissue up to but not into the muscular coat, there were



gonococci massively found, which were in great numbers, both in the pus cells and lying free.

This pathological-anatomical finding is of double interest. Firstly, it shows the intercellular and intracellular wandering of the gonococci in the tissues, and, secondly, that in this case the gonococci had led to an ulcerative process.

Kraus<sup>3</sup> examined eight uterine pus tubes obtained operatively. In one of these gonococci were found in all the layers of the tube wall. The pus from the tube showed, both microscopically and culturally, a pure gonococcic infection. This finding substantiates Wertheim's statement that the gonococcus alone can be held responsible for inflammatory processes in the tubes and the peritoneum.

Wertheim,<sup>4</sup> again, in examination of tissue from a urinary bladder infected by gonorrhœa, found the gonococcus in capillaries and precapillary veins, which he thought they entered by penetrating their walls.

This finding is important, in that it explains the method of general infection by the gonococcus, and thus the gonococcus may be contemplated as only in a degree different from the ordinary pus microbes (Kiefer).<sup>5</sup>

The gonococcus cannot only penetrate tissues, but may lead to abscess formation in them. Menge<sup>6</sup> had found a pure culture of gonococci in an abscess in the wall of the uterus.

But the gonococcus can lead to purely ulcerative processes, as was mentioned in the Frisch case. Jullien<sup>7</sup> calls attention to the finding that, as in the rectum, thus also upon other delicate mucous membranes, the superficial tissues may be exfoliated, owing to the gonorrhœal process, leading even to necrotic ulceration.

The cases of purely ulcerative process called forth by the gonococcus are rare, and, moreover, are exceedingly difficult to demonstrate conclusively. It is not alone sufficient to find a purely gonorrhœal vaginitis, nor even a salpingitis, but the gonococcus should be demonstrated in the tissues themselves. This is difficult, owing to two reasons.

The first is that the tissues must be fresh (Kiefer<sup>5</sup>), owing to the fact that the gonococcus is very short-lived and in a short time disappears. In a few days the gonococcus is to be found only in involution forms, which are very difficult to demonstrate, or are not at all demonstrable in the tissues, as involution forms scarcely stain. For this reason the finding of the gonococcus in tissues does not depend upon the method of staining, but upon the condition of the tissues to be examined. If the gonococci are young and therefore easily stained, their demonstration is affected easily and by all staining methods, even with the ordinary watery solution of methylene blue; if they are old and in involution, they cannot be safely demonstrated by any method.

Again the difficulty arises, that after ulceration mixed infection

easily occurs, and, therefore, other bacteria besides the gonococcus are seen in the tissues, thus apparently vitiating the results of the examination.

The published cases of ulceration due to gonococci are few, and even some of these, for above reasons, are doubtful. Cohn<sup>9</sup> published a case of rupture of a gonorrhœal salpingitis into the intestine. But in this case a purely gonorrhœal process could not be assumed. The following case, however, is positive. Kiefer<sup>10</sup> mentions a case operated upon by A. Martin, similar to the above, which convinced him that an ulcerative process due to gonococci alone is possible. In this case there was a bilateral gonorrhœal pyosalpinx. Both from the cervix and after operation from the pus in the tubes, microscopically and culturally, gonococci alone were demonstrated in the pus in pure culture. At the operation the tubes were so adherent to the rectum that it was impossible to separate them without doing damage to the rectal wall. A small piece, the size of a large coin, about one and one-half the thickness of the normal intestinal wall, adhered to the removed tube. On microscopic section through this musculature there was found, along the blood and lymph vessels, massive infiltration, consisting mostly of polynuclear leukocytes, in which many gonococci were found.

Kiefer thought that this finding makes it highly probable that without the operation in this case also, and in no distant time, a perforation into the rectum would have occurred.

Two cases came to autopsy at Prof. Chiari's institute, which point very probably to the conclusion that an ulcerative process due merely to gonococci was present.

The first case had the following clinical history: O. A., aged eighteen years, a servant, was admitted to the clinic of Prof. von Franquè at the Allgemeinen Krankenhaus of Prag on July 4, 1904, complaining of swelling of the abdomen and obstipation.

At the gynecological examination a discharge from the vagina was noted, pain and infiltration of the parametrium, and a diagnosis of parametritis was made.

On the next day, July 5th, she was transferred to the surgical clinic of Prof. Wölfler. There a diagnosis was made of acute intestinal obstruction, and an immediate operation undertaken.

*Status Præsens.* Of medium height, strong bone structure, well-developed musculature, and fair panniculus adiposus. Mammæ well developed. Percussion of the chest showed no abnormalities. Pulse rapid, small, and of increased tension. Temperature of skin normal.

Abdomen swollen, cone-shaped, mostly at the region of the navel. On pressure great pain was elicited. Percussion, tone was everywhere tympanitic. The area of liver dulness somewhat decreased. Pain distinctly greater in the lower regions of the abdomen.

*Operation, July 5th.* Incision in the median line 10 cm. long. After opening the peritoneal cavity the small intestines, which were

dilated to the size of a man's fist, presented. It was very difficult to keep back the intestines by compression, therefore a rapid search was made for the obstruction. It was seen that the whole jejunum and partially the ileum were dilated almost to rupture; the surface of the serosa was dull in color and in places covered with a sero-fibrinous deposit.

The great omentum was fused into a mass, from which two firm strands extended toward the small pelvis. Several small intestine loops were incarcerated behind the great omentum. The strands were parted, the incarcerated loops freed, and with great difficulty the abdominal wound was closed. Patient, in spite of stimulation, sank after the operation, and died at 3 P.M., July 5th.

*Post-mortem*, July 6th, nineteen hours after death. *Post-mortem* record: Body 152 cm. long, of medium-bone structure, musculature, and panniculus adiposus. The general surface is pale. Posteriorly there are pale livories. Rigor mortis is present. Hair of the head is black. Pupils are moderately dilated and unequal. The visible mucous membranes are pale. The neck and chest are well proportioned. The mammæ are of medium size.

The abdomen is slightly distended. In the middle line, beginning 1 cm. above the navel, there is a wound, 21 cm. long, united by means of button sutures.

The external genitalia are negative.

The soft skull coverings, the skull, meninges, and the brain show no pathological changes.

The diaphragm reaches to the third rib on the right side and to the fourth on the left.

The mucosa of the organs of the neck is discolored. The thyroid gland is of medium size and is negative.

The right lung is fixed slightly. The left is free. The lungs show a dilatation of the alveoli along their margins and are congested in general. In the peribronchial lymphatic glands there are isolated caseous nodules.

In the pericardium there is clear serum. The heart is of normal size, pale and soft. The valves and the intima of the aorta are soft.

The mucosa of the trachea is somewhat reddened, and that of the œsophagus discolored by bile.

In the abdomen there is meteorism of the intestinal loops and reddening of the peritoneum. The omentum reaches over the right half of the abdomen and is adherent in the neighborhood of the symphysis to the abdominal wall. To the left of the symphysis there are remains of adhesions. The left portion of the great omentum lies short and free in the neighborhood of the left flexure of the colon. The small intestines are adherent in part to the abdominal wall, but especially in the small pelvis. The liver is small and pale. The spleen also. The kidneys are pale, but otherwise normal. Their pelves are somewhat dilated.

The urinary bladder is somewhat dilated; otherwise normal. The vagina is negative.

The uterus is visibly enlarged, measuring 7 cm. in length, 4 cm. in breadth at the fundus, and 3 cm. in thickness. The walls are 2 cm. thick in places. Musculature is firm. The uterus is drawn backward by adhesions to the sigmoid flexure. On closer examination of the adnexa of the uterus there is seen behind the uterus a cavity, half the size of a man's fist, isolated and filled with pus, in the anterior wall of which, in numerous adhesions, the tubes and ovaries are enclosed. The pus cavity is 6 cm. broad and 3 cm. deep. The tubes are dilated, their walls thickened, and contain much pus. The ovaries are much enlarged, partly cystic degenerated, and partly pus infiltrated.

In the rectum, corresponding about to the reflection of the peritoneum, on the anterior wall, is a  $1\frac{1}{2}$  cm. long, reddened, somewhat raised, and irregular ulcer. From this yellow pus flows. This ulcer lies behind the uterus  $3\frac{1}{2}$  cm. above the base of the cul-de-sac of Douglas and 13 cm. above the anus. It perforates the rectum from the above-mentioned pus cavity and is seen on the inner wall of the rectum as a pinpoint opening.

The mucosa of the stomach and intestines is pale. Pancreas and the suprarenals are normal.

*Bacteriology.* Pus from the tubes and the pus cavity shows numerous cocci only, not stained by Gram's method, partly intracellular, having the form of semmelcocci.

*Pathological-anatomical Diagnosis.* Salpingitis suppurativa gonorrhoeica bilateralis; pelveoperitonitis suppurativa ulcerosa cum perforatione recti; adhesiones omenti majoris ad parietem anteriorem abdominis in regione symphysis; status postlaparot; miam propter incarcerationem intestini ilei infimi e compressione adhesionibus omenti effecta; peritonitis diffusa incipiens; tuberculosa obolata glandularum lymphaticarum peribronchialum.

The second case had the following clinical history: K. O., aged forty-six years, wife of a laborer, was admitted to the Prager Israelitischen Allgemeinen Krankenhaus on May 19, 1904.

*Anamnesis.* Patient complained of severe pain in the abdomen and of dyspnoea. She claimed to have been always well. Her present illness began about five weeks ago. Without any apparent cause she became ill, complaining of pain in the abdomen, vomiting, eructation, and constipation. Added to the pain in the abdomen, there soon appeared dyspnoea, swelling of the body and feet, which made it necessary to put her to bed.

Patient was pale, sat in bed, dyspnoeic, pulse irregular, unequal, rapid, and about 100 to the minute. Temperature,  $38^{\circ}$  C. Heart action arrhythmic and tones muffled. Heart impulse somewhat external to the mammillary line. The lung findings were those of a bronchitis.

Marked œdema of the lower extremities. Abdomen showed no especial changes. The walls rich in fat.

Palpation everywhere, especially to the left and below, very painful. Liver and spleen not palpable.

*Genital Organs.* Vagina large. Portio enlarged and directed forward. Body and fundus of the uterus enlarged, moderately firm and retroverted, in the left half quite enlarged and tender. This finding was contemplated as a myoma uteri, and disease of the adnexa was not considered. From the uterus a mucopurulent secretion issued.

*Course.* The pains in the abdomen lasted unchanged for some time, then moderated, and finally stopped entirely, as also the fever. The further course was that of an uncompensated heart affection, increasing hydrops, dyspnœa, and oliguria. Death due to œdema of the lungs occurred on July 8, 7.30 A.M.

*Clinical Diagnosis.* Tumor (myoma?) uteri; myodegeneratio cordis; hydrops universalis; hydrops ascites; nephritis interstitialis.

*Post-mortem*, July 9th, twenty-four hours after death. *Post-mortem record:* Body, 165 cm. long, of strong bone structure and musculature, and rich panniculus adiposus.

Skin is pale. Lower extremities are œdematous. Posteriorly there is hypostatic congestion. Rigor mortis is present.

Hair of the head is black, mixed with gray. The visible mucous membranes are pale. Neck and chest are compressed. Mammæ are rich in adipose tissue, as also the abdominal walls, which are pendulous, œdematous, and show many striæ.

The external genitalia show no pathological changes.

Skull is not opened.

The diaphragm reaches on the right side to the fourth rib, on the left side to the fifth rib.

Thyroid gland is enlarged and contains much colloid.

Mucosa of the organs of the neck is pale.

Both lungs are slightly adherent, and there is in both pleural cavities about half a litre of clear serous fluid. The lungs are œdematous, the right somewhat more dense, and in places in the lower lobes atelectatic.

In the pericardium there is a small amount of clear serum. The heart is dilated, especially in its left ventricle. The heart muscle is pale, yellowish, on the right side somewhat spotted. On the left side the papillary muscles of the mitral valves are grayish on section. The musculature of the left ventricle shows many whitish and dark spots. The valves of the left heart show only slight spots of thickening. The aorta shows great unevenness of the surface and many so-called atheromatous ulcers. The openings of the coronary arteries are free; still, the left shows some irregular thickenings in its course. Between the trabeculæ of the left ventricle some pale thrombi are seen.

The trachea and œsophagus are pale. In the free abdominal cavity there are no abnormal contents. The liver is large, firm, and congested. Also the spleen and the kidneys. The surface of the kidneys is scarred. The pelvis of the left kidney is somewhat dilated, and in it there is some urinary gravel.

The mucosa of the pelvis of the left kidney, as also that of the dilated left ureter, is reddened. At the opening of the left ureter into the bladder there is a protuberance of the mucous membrane of the bladder, caused by a dilatation of the lower end of the ureter, the size of a hazel-nut. On the top of this protuberance can be seen the strictured pinpoint opening of the ureter. The bladder is dilated, and the mucous membrane is somewhat reddened. The vagina is normal.

The uterus is enlarged, measuring 9 cm. in length and 4 cm. in thickness at the fundus. Musculature is firm and in places 2 cm. thick. Between the uterus and the rectum is a cavity, half the size of a man's fist, walled off and filled with pus, measuring 6 cm. in depth. The vermiform appendix is also adherent to its upper wall. The tubes are moderately enlarged and filled with pus. The left tube is perforated into the above-mentioned cavity, 1 cm. to the left of the uterus. The ovaries are included in the adhesions and also are partly infiltrated with pus. The anterior wall of the rectum, to the left of the median line, 4 cm. above the base of the pouch of Douglas, and 13 cm. above the anus, is perforated from the pus cavity by a radiating, sharply defined ulcer, measuring 5 mm. in diameter. Corresponding to the base of the ulcer, on the inner surface of the rectum, there is a perforation the size of a pin-head.

The mucosa of the stomach and of the intestines is pale. Pancreas and the adrenals are normal.

Bacteriological examination of the pus from the small pelvis in cover-glass preparations shows, besides many other small cocci, also many diplococci not stained by Gram's method, partly intracellular, in shape semmelcocci, thus gonococci.

*Pathological-anatomical Diagnosis.* Endaortitis chronica deformans; myomalacia cordis multiplex; degeneratio adiposa myocardii; dilatatio cordis totius; vegetationes globulosee in ventriculo cordis sinistro; salpingitis suppurativa gonorrhœica bilateralis, subsequenta pelveoperitonitide ulcerosa circumscrip̄te cum perforatione in rectum; calculosis renis sinistri; dilatatio extremitatis inferioris ureteris sinistri e stenosi ostii ureteris vesicalis; dilatatio ureteris et pelvis sinistri cum ureteritide et pyelitide sinistra.

The first case showed a pure gonorrhœal infection. The second was a mixed infection, which might, however, have occurred by entrance of bacteria from the rectal contents after perforation into the rectum, and the ulceration primarily being probably due to the gonococcus only, as is believed by the writer.

Microscopic examination of both cases showed intense infiltration of the tissues of the tubes, uterus, ovaries, and rectum. Both macroscopically and microscopically, the ulceration was seen to have occurred in the external wall of the rectum and then extended crater-like form into the rectum. Staining for bacteria in the tissues revealed the presence of bacilli, cocci other than gonococci, and a few gonococci in both cases. However, the tissues were examined some time after the post-mortem was performed, and thus, as stated above, gonococci could be found only sparingly and mostly in involution forms, which are difficult or impossible to demonstrate, owing to the fact that they do not stain well, or not at all. The presence of other bacteria may be explained by their entrance into the tissues from the rectum after its perforation. That the ulceration occurred from the outside and not the inside of the rectum is positive by the crater-like form of the ulcer in the wall of the rectum extending from its outer wall inward.

In conclusion it may be stated that the gonococcus can produce ulceration in tissues. For demonstration of this process it is very essential that fresh tissues be examined, and these, if fresh, may be stained with any color medium, even with a simple methylene-blue solution, in order to bring forth the gonococci. A pure culture of gonococci may or may not be found in such cases; but the presence of other bacteria in the pus and in the tissues, after perforation has occurred, may be considered as secondary, provided the original process had been due to the gonococcus alone, and the ulceration, both macroscopically and microscopically, points to a process originating from and not toward the side where the gonorrhœal process primarily existed.

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# THE DIETETIC USE OF PREDIGESTED LEGUME FLOUR, PARTICULARLY IN ATROPHIC INFANTS:

WITH A STUDY OF ABSORPTION AND METABOLISM.<sup>1</sup>

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BEANS and other legumes have throughout many years past been occasionally recommended as useful in dieting infants, and in Germany especially they are said to be a constituent of a number of preparations of "Kindermehl." So far as we know, however, they have been given in a form in which it is impossible for even adults to take considerable amounts without tending to cause more or less digestive disturbance, particularly if they are given for some time; and statements concerning their effects in infants have been based almost entirely upon somewhat loose and casual observations of clinicians or upon the so-called experience of the laity.

The work that we are reporting was carried out partly in order to determine the possibility, in infants that have persistent difficulty in digesting milk proteids, of administering a useful quantity of vegetable proteid in a form suited to their digestion. We also investigated the question whether this proteid in its influence upon metabolism shows any important differences from milk proteids that are dependent upon the character of the proteid as distinguished from its digestibility and from the mere fact that it is proteid food.

Our results have shown the feasibility of successfully administering vegetable proteid to infants in considerable amounts and for at least a fairly long period. They also suggest that the favorable influence upon nutrition observed in a large proportion of cases is more largely referable to the character of the proteid that we used than to the amount, though this is a point that necessarily has in it an element of undemonstrable theory, and that can be provisionally accepted only after further control studies.

The investigation of the use of vegetable proteid in infants was undertaken at the suggestion of Dr. J. P. Crozer Griffith. The coincident consideration of the probable dependence of the nutritional improvement that occurred in a large proportion of the cases studied, upon the character of the proteid, we based upon the following theoretical grounds: Native food proteids are of various kinds, the chief among them being albumin, nuclealbumin, nucleoproteid, and a

<sup>1</sup> Read by invitation before the Buffalo Academy of Medicine, December 13, 1904.



less important group most satisfactorily called albuminoids. Albumins, represented for example by egg-albumen, are distinguished by a series of reactions, but, for our purposes, particularly by the fact that they do not contain phosphorus compounds. Nucleoalbumins, conspicuously represented by casein, are especially distinguished by the fact that they contain phosphorus compounds, but do not yield any xanthin bases upon disintegration. Nucleoproteids, represented among animal foods most strikingly by various organs rich in cells, such as the pancreas and the thymus, but found also widespread in the vegetable kingdom, are distinguished chiefly by the fact that they contain a large amount of phosphorus compounds and do yield xanthin bases upon their disintegration. The albuminoids are represented by gelatins and a series of other substances which are of less specialized form than the substances mentioned above.

In human or other animal tissues the protoplasm of the cells is made up largely of albumin, in some cases of nucleoalbumins also; while the nuclei of the cells are formed chiefly of nucleoproteid. Adults receive in their food, in addition to albumin and nucleoalbumin, considerable quantities of nucleoproteid. It is not known how they manufacture the nucleoproteid of their tissues, but it is at least not improbable that the nucleoproteid of the food, or at any rate the nucleic acid that this nucleoproteid contains, is used for a part or the whole of this process. This would at any rate appear to be an economical method as compared with the wholly synthetic manufacture of nucleoproteid from relatively simple substances. In infants, however, the cell nucleoproteid must be manufactured, for the food contains no true nuclein, the proteids of the milk being entirely albumins and nucleoalbumins. If, then, the adult uses his nucleoproteid more or less directly in cell construction, the infant has in this point greater complexity in its metabolism than the adult; and it is possible that this is one reason that the assimilative powers of an infant are so much more subject to uncontrollable breakdown than those of an adult. It seemed possible, therefore, that when the assimilative functions are already incompetent it might be feasible to help the child by giving it nuclein in a form that would be readily absorbed without disturbing the digestion. The difficulties in the way of using animal foods for this purpose in noteworthy amounts are too great, but vegetables of the class of the legumes (beans, peas, lentils) contain extremely large amounts of nitrogenous substances and among these there is a considerable amount of nucleins. That starch can be given to infants in large amounts if predigested is known, and this fact has been used in a special manner by Keller, for example, with apparently very successful results. There was, therefore, no evident obstacle in the way of the use of legume flour except the possibility that the proteid that it contains might disturb the digestion. Heating, however, causes much of this proteid

to go into solution if it is finely ground, and, from a mechanical standpoint, the remainder would appear to be at least no more disturbing than the easily coagulated milk proteid. The practical effects of its use remained to be determined.

In studying this question we have given predigested bean flour to a series of infants, having first convinced ourselves, by the administration of small amounts of the bean flour, that it did not disturb digestion, and having also first studied its absorption and determined that this was, in the infants investigated, satisfactory.

We will discuss first the method of preparing the flour and the manner in which it was used, and then refer briefly to the studies of absorption and metabolism, subsequently discussing the clinical results.

We were unable to find on the market any satisfactory bean flour or pea flour. We, therefore, secured white kidney beans, dried them, and in our first experiments ground a few pounds of flour ourselves in an ordinary spice mill, removing the shell, and using only very fine flour secured by bolting; subsequently we had about two hundred pounds ground for us. It is essential that the flour should be finely ground in order that it may be subject to satisfactory predigestion, and also in order that the proteid may be properly absorbed. There has been much discussion of the question whether vegetable proteid is well absorbed or not (in adults). It seems probable that the correct answer to this question is that unfavorable results are due to the form in which the vegetable proteid is administered. The studies have usually been made with vegetables cooked in the ordinary manner, and in this form the proteid is enclosed in large part in a tough mass of cellulose. Rockwood has shown that, if administered free from cellulose, vegetable proteid is well absorbed. It is, therefore, important to see that the flour is finely ground. The object of predigestion was, of course, to convert the starch, the method of preparation having no effect upon the proteid excepting that due to the heat. In our work we usually prepare a 10 per cent. solution of predigested bean flour, first mixing the weighed or measured bean flour with water until made into a smooth paste, then adding more water until it can be easily stirred, and then heating in a double boiler at a good heat for fifteen or twenty minutes, stirring very frequently. During this time the flour of course swells and a 10 per cent. mixture of flour and water becomes a rather thick paste. It is then cooled to between 60° and 70° C., and the ferment is added and allowed to act for about ten minutes, stirring the mass frequently and loosening the portions that have adhered closely to the sides of the vessel so that they may undergo thorough digestion. Within a few moments after adding an active diastatic ferment the mass becomes perfectly fluid and resembles a rather thin soup. After this, in order to stop the action of the ferment, it is brought to the boiling point; it is then

cooled and is ready for use. The ferment that is to be used is largely a matter of choice, the only essential being that the ferment shall be active and in convenient form. We generally used cereo, sometimes maltine. Any of the other good diastatic ferments on the market would probably do as well. We have used the first mentioned chiefly because it is in very convenient form for this individual purpose and is very active. The nature of the mixture after the digestive process is past has not been investigated farther than to determine that there is little, if any, iodine-reacting starch present and that practically all the flour is in a fluid form. The proteid present would seem from the physical standpoint to be in a condition very suitable for absorption, for it is largely in solution, the solid particles that remain are few and extremely small, and it is impossible to bring down any coagulum by heating, while even strong acids precipitate the proteid only in the form of fine flakes.

In using this preparation with infants we have done as follows: A quantity of the infant's milk mixture approximately equal in food value to the amount of bean flour that we were about to add was discarded and was replaced by 10 per cent. solution of bean flour. For example, with a 3.6.1 milk mixture, the 10 per cent. bean flour is somewhat less than a direct equivalent of an equal quantity of the milk mixture; therefore, in such a case we gave the food as follows: if the child was receiving 48 oz. of 3.6.1. per day this was reduced to 36 oz., and 15 oz. of 10 per cent. bean-flour solution was added; the child therefore got 51 oz. a day, but received about the same energy value (actually slightly less) in its food. In a good deal of the work bean flour was not added at one time to the total quantity of the day's food, but was kept separate and a proper amount was added to each feeding. For example, with previous feedings of 4 oz. of 3.6.1. mixture the child was now given 3 oz. of 3.6.1. and  $1\frac{1}{4}$  oz. of 10 per cent. bean-flour solution. In almost all our work with infants the feedings contained 2.5 per cent. to 3 per cent., at most, of bean flour. From the determinations that we made of the nitrogen in the flour, which will be mentioned immediately, we found that 3 per cent. of bean flour meant about 0.65 per cent. of proteid.

We made, in all, five analyses of the nitrogen in the bean flour. They resulted as follows: I., 3.447 per cent.; II., 3.448 per cent.; III., 3.394 per cent.; IV., 3.559 per cent.; V., 3.327 per cent.; the average being 3.435 per cent. of nitrogen, or 21.468 per cent. of proteid.

In our absorption work we used diapers made of rubber tissue, large wads of absorbent cotton being placed over the genitals to avoid any mixture of the urine with the feces. By this method we could collect the feces on the rubber diapers with entire success and without loss. The only difficulty that we had was that in one instance, when the observations were continued for ten days, the child had rather marked irritation of the skin about the buttocks.

In the one instance in which we did a complete nitrogen metabolism experiment in an infant, we collected the urine by introducing the penis into a piece of rubber tubing, strapping the tubing on with adhesive plaster, the lower end of the tubing discharging into a vessel which collected the urine. In the metabolism experiment in an adult we followed the customary methods. In the case of the infants the nitrogen in the food was determined each day. In the experiment with the adult we used a diet containing substances of which we had many times estimated the nitrogen-content ourselves, or which have a well-known and practically constant nitrogen-content.

The results of our absorption experiments in infants were as follows: Case I. was a boy, aged six months when studied, who had been in the house three weeks, and in this time had gained and lost repeatedly an ounce or two at a time. When the study was begun he weighed six pounds fifteen ounces. He had usually three soft bowel movements daily that were fairly satisfactory. In the preliminary period of study the child received 4 oz. of 4.7.2. mixture every three hours. This period of study was three days in length. The child was then put on 3 oz. of 4.7.2. mixture and  $1\frac{1}{4}$  oz. of 10 per cent. bean-flour solution every three hours, and the absorption was studied for a period of six days following. In the two periods the conditions of nitrogen absorption were as follows:

PRELIMINARY PERIOD.		BEAN-FLOUR PERIOD.	
Received in three days . . .	8.601 gm.	Received in six days . . .	19.111 gm.
Average daily . . .	2.867 "	Average daily . . .	3.185 "
Excreted in feces in three days . . .	0.503 "	Excreted in feces in six days . . .	1.203 "
Average daily . . .	0.167 "	Average daily . . .	0.200 "
Absorption in three days . . .	8.098 "	Absorption in six days . . .	17.908 "
Average daily . . .	2.699 "	Average daily . . .	2.984 "
Absorption of the intake . . .	94.2 %	Absorption of the intake . . .	93.7 %

The second case was studied at the same time and in the same way. The same amounts of food were given in both periods, but the child vomited about two ounces after one feeding; therefore, the intake in the preliminary period was slightly less than in the first case. This child was four months old when studied; had been in the house six weeks, and had varied between six pounds thirteen and one-half ounces and seven pounds three ounces, and showed the latter weight when the bean flour was begun. There were three or four bowel movements daily, which were yellow, quite well digested, but contained a little mucus. The conditions of nitrogen absorption in this case were as follows:

PRELIMINARY PERIOD.		BEAN-FLOUR PERIOD.	
Received in three days . . .	8.422 gm.	Received in six days . . .	19.111 gm.
Average daily . . .	2.807 "	Average daily . . .	3.185 "
Excreted in feces in three days . . .	0.415 "	Excreted in feces in six days . . .	0.548 "
Average daily . . .	0.138 "	Average daily . . .	0.091 "
Absorption in three days . . .	8.007 "	Absorption in six days . . .	18.563 "
Average daily . . .	2.667 "	Average daily . . .	3.093 "
Absorption of the intake . . .	95.1 %	Absorption of the intake . . .	97.2 %

In these two cases the absorption was very good in both periods. In the first case there was only a fraction of 1 per cent. difference in the two periods; in the second case absorption during the bean-flour period was better than during the preliminary period. These figures show that in these children the bean proteid was fully as well absorbed as the milk proteid, and both were extremely well absorbed.

In another child we investigated both absorption and metabolism while bean flour was being given. We had no opportunity to study a control period when the child was taking only milk. The figures for the period of investigation, which was five days in length, are as follows:

Received of nitrogen in five days . . . . .	14.480 gm.
Average daily . . . . .	2.886 "
Excreted in feces in five days . . . . .	1.844 "
Average daily . . . . .	0.368 "
Absorption in five days . . . . .	12.586 "
Average daily . . . . .	2.517 "
Absorption of the intake was therefore . . . . .	87.92 %

This child's urine was studied daily, with the following results:

First day . . . . .	0.3192 gm. nitrogen.
Second " . . . . .	0.2240 " "
Third " . . . . .	0.1032 " "
Fourth " . . . . .	0.1041 " "
Fifth " . . . . .	0.3032 " "
Total in five days . . . . .	1.0597 " "
Average in one day . . . . .	0.2119 " "
The nitrogen in the food was . . . . .	14.4305 gm.
" " feces " . . . . .	1.8441 "
" " urine " . . . . .	1.0597 "
Total loss through excretions was . . . . .	2.903 "
Total retention was . . . . .	11.527 "
The retention of the intake was . . . . .	79.87 %

Whether these figures relating to the child's metabolism are wholly reliable or not cannot be said. Some studies of infants in the first few weeks of life have shown extremely high grades of nitrogen retention as compared with those that are observed in adults, even exceeding the retention shown by our figures in this case. This is natural because of the very rapid growth of their tissues at that period, but 79.8 per cent. of retention is so astonishingly high for an infant of the age of our subject that we cannot help suspecting that some of the child's urine was lost. If it was, we could not discover it, a careful watch having been kept on the apparatus regularly without any evidence of loss of urine at any time during the experiment. We do not feel, however, that the figures for metabolism can be further commented upon than to say that if they are correct they show most unusually favorable conditions, particularly for an atrophic infant. The figures for absorption are much poorer than those in the other children and

are not very satisfactory. This was expected in this child, as he came in with a good deal of digestive disturbance, with about five movements daily, which were greenish and contained many curds. The bowels improved after his admission, but this study was begun soon after he came in, when there was still some digestive disturbance.

The further study that we made of metabolism and absorption was carried out in an adult patient, a subject of phthisis. This man had been on a very free diet, having had three meals a day and as large a quantity of milk and raw eggs in addition as he cared to take. He had been gaining quite rapidly in weight on this diet, and his general condition had improved. Because his previous diet had been a very heavy one, we put him, in both the preliminary and bean-flour periods, upon a very free diet as to quantity. In the preliminary period this consisted of milk 2400 c.c.; rice, 30 gm.; eggs, eight daily; bread, 300 gm.; butter, 60 gm.; sugar, 30 gm.; steak, 200 gm.; baked potato, 70 gm. In the bean-flour period the diet remained the same, excepting that the milk was reduced by 550 c.c. each day and in its place he was given each day a solution of predigested bean flour which contained 100 gm. of (dry) bean flour. The nitrogen in the food was estimated by weighing accurately each portion of the food and calculating the nitrogen from the weights. We have ourselves made a large number of nitrogen estimations of the bread, milk, butter, and steak used in the hospital in previous metabolism experiments that we have carried out, and we took the average of these figures for these foods. The nitrogen of the eggs and rice, which is very constant for a given weight, we took from the tables of König and Blyth. The nitrogen excreted in the urine was estimated daily. That of the feces was estimated in the total amount after the feces had been collected throughout the proper period, dried on the water bath (sulphuric acid having been added) and then ground fine. One detail of the work on the feces may be of some interest to investigators in this line. We have repeatedly had the experience, as we had in this instance, of finding that feces contained so much fat that it was impossible to grind them fine after drying them, or to get a homogeneous mixture by occasional stirring while they were drying. We have in some instances overcome this by extracting with alcohol and ether, then drying and grinding the residue and making nitrogen (and when desired, fat) estimations of both the residue and the alcohol and ether extracts. This burdensome procedure, however, proved unnecessary in this instance, and very good results in control estimations were obtained by first extracting with alcohol and ether, then grinding the residue fine after drying it, and then adding the alcohol and ether extracts again to the ground residue and evaporating as quickly as possible, with constant stirring so as to keep the mass thoroughly mixed. In this way a homogeneous mixture was

obtained, and it could also be ground in a mortar much finer than it could before. Control estimations of the nitrogen corresponded very closely.

The results in this case were as follows:

#### PRELIMINARY PERIOD.

			Nitrogen in the Food.	Nitrogen in the Urine.
October	31	. . . . .	33.0347 gm.	25.4710 gm.
November	1	. . . . .	33.7943 "	23.1336 "
"	2	. . . . .	32.7100 "	22.1450 "
"	3	. . . . .	33.1116 "	21.0112 "
"	4	. . . . .	32.2051 "	25.5780 "
"	5	. . . . .	33.1345 "	18.8160 "
"	6	. . . . .	32.1041 "	21.1232 "
Total		. . . . .	230.0043 "	157 2780 "
Average		. . . . .	32.8577 "	22.4682 "

The total nitrogen in the feces in this period was 12.1866 gm.; the average daily excretion in the feces was 1.7409 gm. The combined urinary and fecal nitrogen in the whole period was 169.4646 gm.; and the daily average excretion was, therefore, 24.2092 gm. Since then the daily average in the food was 32.8577 gm., the average daily retention was 26.3 per cent. of the intake. The absorption of nitrogen was 93.7 per cent. of the intake.

#### BEAN-FLOUR PERIOD.

			Nitrogen in the Food.	Nitrogen in the Urine.
November	7	. . . . .	30.3704 gm.	22.3264 gm.
"	8	. . . . .	27.5247 "	17.1888 "
"	9	. . . . .	28.6844 "	23.7832 "
"	10	. . . . .	30.7284 "	21.7140 "
"	11	. . . . .	32.4540 "	18.2564 "
"	12	. . . . .	33.2469 "	22 9600 "
"	13	. . . . .	33.9411 "	17.3600 "
"	14	. . . . .	33.2166 "	29.9880 "
"	15	. . . . .	32.9460 "	21.7728 "
Total		. . . . .	283.1125 "	195.2796 "
Average		. . . . .	31.4569 "	21.6977 "

The nitrogen in the feces in this period was 17.0581 gm.; the daily average was 1.8953 gm. The combined urinary and fecal nitrogen was 212.3377 gm.; the daily average excretion was 23.5937 gm. The daily average in the food was 31.4569 gm. Hence, the average daily retention was 7.8639 gm. and the total retention was 70.7748 gm., which was 24.9 per cent. of the intake. The absorption in this period was 94.0 per cent. of the intake.

These figures for metabolism are, therefore, somewhat against the bean flour, since the retention, which was high in both periods, was about 1.5 per cent. better in the preliminary period than in the bean-flour period. The conditions in the early part of this experiment were, however, not satisfactory, for we met the same difficulty that has been noted many times before in attempts to administer legumes as ordinarily cooked, over a considerable period con-

tinuously; that is, after the first few portions, the man objected so greatly to the taste that it was almost impossible for him to take the beans. He made a willing effort to do so, however, and succeeded; but it upset his appetite so much that he was unable to take the proper amount of the other food, as is readily seen by referring to the table for the food nitrogen in the bean-flour period. These figures drop decidedly on the first day, and much more in the next two days; rising again on the next day, and reaching the proper point on the fifth day. The explanation of these figures lies in the point noted; in the first three days it was impossible by any of the means that we used to flavor the beans so as to make them agreeable. The rise in food nitrogen on the fifth day was coincident with the use of cinnamon as a flavor; this was agreeable to the man, and subsequently throughout the period of investigation and a long period afterward he took the predigested bean flour in his milk with entire satisfaction. The last five days of the experiment, therefore, offer a fairer comparison with the preliminary period than does the whole bean-flour period. The figures for these five days are as follows:

Average daily food nitrogen	. . . . .	33.1609 gm.
Average daily urinary nitrogen	. . . . .	22.0534 "
" " fecal	. . . . .	1.8953 "
Total excretion daily	. . . . .	23.9487 "
Average retention (27.4 % of the intake) was	. . . . .	9.2122 "
Absorption of the intake was	. . . . .	94.2 %

The figures in this part of the bean-flour period are, therefore, 1 per cent. better as regards nitrogen retention than in the preliminary period, and almost 3 per cent. better than in the total bean-flour period. The figures for absorption in this period are very slightly below those in the preliminary period, but the figures for absorption in all three of these periods are so similar that they provide sufficient evidence that this man absorbed the bean nitrogen practically as well as the nitrogen from the milk, eggs, steak, and bread. All were absorbed very satisfactorily, particularly considering the very large food intake.

We cannot draw very definite conclusions from this experiment excepting to say that the bean proteid was quite as satisfactory as the other proteids in its influence upon metabolism. In the last part of the bean-flour period it seemed to have a slightly better effect upon metabolism than the other proteids, though the difference is so slight that little weight can be laid upon it. We could not expect much difference, however, even if nuclein has a noteworthy influence upon proteid metabolism as compared with the influence of other forms of proteid, for this man was already getting some animal nuclein in his food. The experiment serves chiefly to demonstrate the entire metabolic suitability of a large quantity of



legumes in maintaining a large nitrogen retention, and also the satisfactory absorption of the proteid in the legume. The last result directly supports the view previously referred to concerning the absorption of vegetable proteid, and the results with metabolism also support the observations that have been made in considerable number, in adults, in regard to the influence of vegetable diet upon nitrogen metabolism, most such experiments having demonstrated the ready possibility of maintaining a nitrogen equilibrium and of sometimes producing a nitrogen retention, on a vegetable diet. This was usually done, however, by using vegetables cooked in the ordinary manner. The preparation that we used has the advantage of being an extremely concentrated food containing a very high energy value for its bulk and it is at the same time in fluid form. It is, therefore, in these points an excellent food for improving the nutritive condition when it is impossible to take a large bulk or to take solid or semisolid food in considerable quantities. The chief difficulty with it, and one that has as yet been hard for us to overcome, is the flavor, which is distasteful to most adults and older children from the beginning, or soon becomes so. Infants take it without trouble in practically all cases after one or two feedings, but it is difficult to persuade older children and adults to do so. Attempts to accomplish this become largely a question of flavoring, but when flavoring ingredients are necessary over a long period of time a great variety must be used or they too become distasteful. This limitation of the usefulness of this food in older persons may, therefore, remain permanent. The point cannot now be settled.

In infants, however, our clinical results up to the present have been such as to encourage us decidedly. We have not as yet used it in a very large series of cases, as our attention has been chiefly directed to the determination of its influence upon absorption and metabolism, and during this particular period of the year we have not had a large number of cases available for study. Those that have been studied are the following: nine in the service of Dr. Griffith at the University Hospital; five at the Seashore House at Atlantic City studied through the kindness of Dr. William H. Bennett; one private case of Dr. Charles H. Schoff. In these cases the gentlemen who had charge of the cases, or their assistants, usually the latter, prescribed the diet, excepting only that we suggested the amount of bean flour to be used. Another series, that could be studied for only a brief period, was seen at St. Christopher's Hospital. The results in the first fourteen cases, briefly abstracted, are as follows, first mentioning the least favorable cases:

CASE I.—J. P., aged five months; weight ten pounds nine ounces. Treated at Children's Seashore House, Atlantic City. Lost weight for ten days continuously, but slowly. Then weighed ten pounds four ounces. Had been on Meigs' mixture, then on partially peptonized milk. Was put on whey upon the appearance

of decided acute digestive disturbance, in which the stools became green and contained mucus and curds and occasionally a trace of blood. This continued and he was put by one of the residents on three parts of Meigs' mixture and one part of 10 per cent. predigested bean flour, giving three ounces of this mixture every three hours. No noteworthy change occurred in his condition, and after ten days he was taken home, having lost in all one pound from the time of his admission. In our view this case was at this period an unsuitable one for this food or any other except the most dilute.

CASE II.—L. C., a girl aged ten months; weight nine and one-half pounds. Admitted to Children's Ward, University Hospital, with three or four greenish stools daily, containing curds. No acute disturbance. Put on barley-water for twenty-four hours. Then on a 3.6.1. mixture, three parts; 10 per cent. bean-flour solution, one part; five ounces being given every three hours.

The stools rapidly became normal and the child in ten days gained exactly a pound. At this time it developed fever, cyanosis, and rapid respirations. There was no digestive disturbance for five or six days after the onset of this acute illness, when a mild diarrhoea developed and the child one day vomited. The diet was then changed to a plain milk mixture without any noteworthy change in the condition of the digestion; the cyanosis and rapid respiration also continuing. This child died after continued illness. This case is mentioned among the unfavorable ones because one or two of those who saw the child thought that the bean flour was responsible for the acute illness. We personally felt that the attack was not originally a digestive one at all, but was probably due to an obscure bronchopneumonia. Autopsy showed numerous pyæmic abscesses of the lungs originating in middle-ear disease. This case cannot be used for or against the bean flour, though the child temporarily gained very rapidly on the mixture containing bean flour.

CASE III.—J. O., aged three months; weight eight pounds one ounce. Admitted with greenish stools containing curds; five movements daily. This child was the one mentioned as having been studied as to both absorption and metabolism. After one day of barley-water, the child was put on three parts of 4.6.2., one part of 10 per cent. bean-flour solution; why the diet was increased suddenly to this point is not recorded. In the next six days the child gained six ounces; it had never gained as much before. The bowel movements after the first two or three days became soft, yellow, and contained no curds, but there were three or four movements a day. In the following nine days he gained but one ounce more and the bowels were the same. On October 4th he had not gained further and the mother took him home. A more gradual increase in the food might have been more successful.

The others of the cases that were treated at the University Hospital and at Atlantic City are all more or less favorable. We will mention first the University Hospital cases and then the Atlantic City cases.

CASE IV.—Girl, aged four months; weight six pounds thirteen and one-half ounces. This child was the second of our absorption studies. She was admitted having three or four movements a day; they were yellow, half-formed, contained a little mucus. She had lost weight gradually since birth, and had at no time gained; was extremely emaciated and weak. Upon admission she was put on barley-water, followed by Keller's malt-soup; after a week this was changed to a simple milk mixture, containing barley-jelly, which was afterward malted. As the bowels improved, the milk mixture was increased to a 4.7.2., containing malted barley-jelly. Throughout six weeks her weight had varied, with slight rises and falls, between six pounds thirteen ounces and seven pounds three ounces. Bean-flour solution was then added to the 4.7.2. mixture; her weight at this time being seven pounds three ounces. Six days later our bean flour gave out; at this time she weighed eight pounds. She continued gaining after this for four weeks, when she weighed nine and one-half pounds, a simple 4.7.2. mixture having been used during this time. She then lost half a pound in a week, and regained it only very gradually in the next three weeks. This was at the beginning of summer, and her slow gain was thought to be due to hot weather and "hospitalism," and she was sent to the seashore.

CASE V.—The first of our absorption experiments. Was admitted with three to five stools daily that were greenish and loose. He was six months old; weighed six pounds fourteen ounces. He was much emaciated and weak. He was put on barley-water and then on weak milk mixture; gradually increased as the bowels soon became nearly normal to a 4.7.2., which was ordered eleven days after he was admitted. Eighteen days after admission his weight was six pounds fifteen ounces, there having been only slight fluctuation in this period. He was then given bean flour in the 4.7.2. mixture. Six days later, when the flour gave out, he weighed seven pounds fourteen ounces, the bowels remaining the same. Afterward, on a simple 4.7.2. mixture, he gained gradually, in five weeks, to nine and one-half pounds. He was then taken home in satisfactory condition and was lost sight of.

CASE VI.—L. D., aged four months; weight six pounds; very weak. Admitted with mild digestive disturbance; three to five stools daily, which were yellow and partly formed, but contained some curds. Put on barley-water, then on dilute milk mixture, gradually increased. Five weeks after admission was given 4.7.2. mixture. The child was then having two or three movements a day, which were yellow and quite well digested, but there had been

no gain. Six weeks after admission was given bean-flour solution in the 4.7.2. mixture. Four days later she weighed eight and one-half pounds. Was taken home just after this, weighing eight pounds nine and one-half ounces. Readmitted a week later with loose, greenish stools, and having lost half a pound; she had been on a simple milk mixture outside the hospital. Was put on barley-water, then on her previous milk mixture, and gained half a pound in five days. After this stayed stationary for a week and was then given bean-flour solution again, in her milk mixture, and gained a half-pound in four days, and a quarter of a pound in the next five days, and was again taken home in satisfactory condition, weighing nine and one-quarter pounds. The gain in this case when bean-flour solution was first given was almost incomprehensible. At each weighing before this time the record had been within an ounce or two of six pounds. At each weighing after five days of bean-flour solution the record was regularly above eight and one-half pounds. She was carefully weighed by the nurse, the resident physician, and by one of us, all records agreeing. The scales may have been at fault, but they were correct when tested afterward. If the gain was as recorded it was certainly not all due to increase of tissue, for in all her food during this time she received a little less than enough solids to have made this gain if all had been deposited in the form of tissue. Hence, some of it must have been retention of water. Water retention, however, is a very desirable thing in most atrophic infants, as their tissues are usually very abnormally dry. Whatever may be said of the weight records, the improvement in the child's condition was perfectly astonishing; within four days she became a wholly different-looking infant, and she retained her improvement.

CASE VII.—Girl, aged thirteen months; weight eleven pounds, one ounce; very ill-nourished and weak. Admitted with five or six greenish stools daily, which contained mucus. Put on barley-water and then on a milk modification which was increased to 4.7.2. mixture, although the stools remained about the same. She gained a half-pound in the first ten days; then remained stationary for a week. Was then put on bean-flour solution. The bowels improved, but the movements still remained greenish and loose for a week, and in this time she lost a half-pound. From this period on, however, the bowels rapidly improved and soon became normal, and in the next three and one-half weeks she gained one and one-half pounds, and was discharged weighing one and one-half pounds more than when admitted, her bowels for two weeks having been entirely normal.

CASE VIII.—C. B., girl, aged six months; admitted weighing seven and one-half pounds, with three or four greenish, half-formed movements daily. Put on barley-water for twenty-four hours, followed by simple milk modification. Bowels did not improve,

and the child lost a half-pound in four days. Bean-flour solution was then added. The bowels within three days became normal, and in ten days the child gained slightly over a half-pound; in five days more another half-pound; in three days more another half-pound. Was discharged, with normal bowels, weighing eight and one-half pounds.

CASE IX.—D. L., boy, aged seven months. Admitted weighing nine pounds, with four or five movements daily, which were green and contained mucus and an occasional trace of blood. Put on barley-water, then on milk mixture; the bowels improved at first, but after three days remained stationary, continuing loose and greenish, with some mucus. Nine days after admission the child was on a 4.7.1. mixture; weighed nine and one-half pounds, but had been stationary for nearly a week. Then bean-flour solution was added; three days later the bowels were recorded as nearly normal, the child still weighed nine and one-half pounds. Six days later had gained a half-pound; four days later another half-pound; four days later than this another half-pound. Was discharged in satisfactory condition.

CASE X.—K. D., boy, aged nine months; weight twelve pounds; ill-nourished and weak. Three to five yellowish stools daily, containing curds. Put on barley-water and then on milk mixture, which was increased to 3.6.1. mixture and afterward up to 4.7.2. He had gained three ounces in five days. Wheat flour, predigested as the bean flour had been, was then added. The child gained four ounces in four days; then remained stationary for three days. Then predigested bean flour was substituted, and in the next three days there was a gain of nine ounces; in the next week four ounces; in the next week twelve ounces. Was discharged weighing fourteen pounds. The bowels had improved on the milk mixture and remained in good condition with the use of both wheat flour and bean flour.

The following four cases were treated at Atlantic City, by Dr. Wm. H. Bennett and Dr. Sidney Repplier:

CASE XI.—E. W., girl, aged seven months; weight fourteen pounds four ounces. Stools fairly normal; weight decreased regularly for a week, during which time she lost half a pound. At that time the bowels became loose, contained mucus, and were greenish. She had been on Meigs' mixture. To this was added, through a misunderstanding, over 4 per cent. of bean flour, with the result that vomiting occurred after every feeding. She was then put on peptonized milk and two days afterward was put back on Meigs' mixture containing  $2\frac{1}{2}$  per cent. of bean flour. Her weight was then thirteen pounds; stools greenish and contained mucus and curds. One week later had lost four ounces, but the stools were improved. Three days later gained two ounces, stools much improved. One week later gained five ounces, stools normal;

four days later gained five ounces more, stools normal. Was then taken home in good condition.

CASE XII.—Boy, aged five months; weight ten pounds eight ounces. Stools greenish and loose. Lost on Meigs' mixture six ounces in a week. Was then given  $2\frac{1}{2}$  per cent. bean flour in Meigs' mixture. Three days later stools much improved, had lost two ounces; three days later stools normal, had gained four ounces. Was then taken home by the mother.

CASE XIII.—A. E., aged seven months; weight twelve pounds; stools greenish, with curds. On Meigs' mixture, from July 1st to 26th, lost a pound. Bowels remained bad. Put, through misunderstanding as in the first case, on excessive amount of bean flour, getting over 6 per cent. Vomited occasionally for a day. Amount of bean flour reduced to  $2\frac{1}{2}$  per cent. Vomiting stopped at once, stools improved rapidly. Three days later stools normal excepting for a little mucus; had gained nine ounces; three days later had gained seven ounces more. Stools normal. Developed chicken-pox and was sent home.

CASE XIV.—E. H., aged six months; weight eleven pounds four ounces; stools normal. Gained four ounces in a week; stools then became loose, and contained a little mucus. Lost six ounces in ten days. Had been on Meigs' mixture. Then bean-flour solution added. Gained four ounces in three days; stools improved. Gained ten ounces in the next five days; stools normal. Discharged in good condition.

In addition to these cases there were treated at St. Christopher's Hospital, in the service of one of us (Edsall), thirteen infants (Cases XV. to XXVII., inclusive), who for a short time got milk mixtures containing predigested wheat flour or predigested bean flour, the wheat flour having been used at first because bean flour could not be secured at that time. Unfortunately bean flour was obtained only a very short time before the term of duty on this service was ended, and hence these observations are of little value. They serve chiefly as a contrast between the effects of wheat flour in these cases and of bean flour in the cases that have already been detailed.

Of the thirteen cases, six were treated with mixtures containing predigested wheat flour, but got no bean flour, receiving the wheat flour in various cases for from ten days to three weeks. Five of these six lost persistently; one gained nicely from five pounds twelve ounces to six pounds twelve ounces in ten days, after having lost for the preceding ten days. The bowels in this case remained slightly loose. Three other infants got wheat flour for from ten days to two weeks, one gaining a few ounces at first and then losing, the others losing persistently. When bean flour was secured all these three were apparently near death, and all ultimately died; but upon the use of bean flour one held its weight for a week and then rapidly lost, while the others gained four ounces each in the first

three days, and then died unexpectedly without any new symptoms. In all these cases the bean flour seemed to be well digested, and in all of them the bowel movements became more satisfactory under its use. Two other infants that had been on predigested wheat flour showed decided improvement of the bowels under bean flour, but were sent to the seashore in three days after its use without any record of their weight at the time. Another child had lost rapidly on predigested wheat flour and showed no gain on bean flour, though it held its weight for a week, when it suddenly died. It seemed *in extremis* when bean flour was started. Another child came in with a mild acute enterocolitis. It got barley-water for forty-eight hours, then whey, afterward whey and albumin-water alternating. The bowels remained persistently bad for a week, and the infant lost a pound. It was then given whey with  $1\frac{1}{2}$  per cent. of fat added and 2 per cent. predigested bean flour. The bowels became normal almost at once, and the infant gained a pound and a quarter in three days, and was taken home by its mother and lost sight of.

In none of these cases, excepting the last, was the child in a condition that permitted of any special hope from any treatment at the time that bean-flour solution was started. The results with wheat flour (that was given in almost the same form that Keller gives it in his malt-soup; though it was digested with another ferment) were very unsatisfactory in eleven out of twelve instances. One child, as stated, showed rapid improvement, but the others lost persistently, and no very satisfactory influence upon the bowels was observed; though in no instance did it seem to produce any further digestive disturbance. Hence, the results with wheat flour appear to be much less satisfactory than those with bean flour, though it is, of course, not wholly fair to contrast a group of cases in one institution with those in another. On the whole the St. Christopher's cases were more advanced when the wheat flour was started than were most of the cases at the University Hospital or at Atlantic City that were on bean flour; but in none of the cases at St. Christopher's Hospital was there any very recent acute disturbance of the digestive tract, excepting in the one last described. All the cases, including the last, were atrophic infants, their weights ranging from five and one-half to nine pounds. Three of the infants were under ten weeks of age; one of these was the infant that gained rapidly on wheat flour; the other two did not gain. One other was four months old, and the remainder were between six and eleven months of age.

In addition to atrophy in infants, we have thought that predigested legume flour might be of value in the management of cases in older children or in adults in which there is persistent digestive disturbance and difficulty in taking a sufficient amount of food, particularly proteid food; or in which there is malnutrition from other causes, and the food intake is unsatisfactorily low.

Our observations on this point have been as yet very fragmentary and we do not now feel extremely hopeful in regard to its practical usefulness in most of such cases unless some means of flavoring it satisfactorily can be devised; for, as stated, adults and older children object at once, or after taking a few portions, to the taste of the beans. The man on whom we did the metabolism experiment gained four pounds in the preliminary period (that in which no bean flour was used). In the first four days of the use of bean flour, when his appetite was much upset, and he took a much reduced amount of food, he lost two pounds; but in the next five days he gained three pounds, so that the gain in the first period and the last part of the bean-flour periods was practically the same. Afterward he went back to his usual diet and lost a pound a week for two weeks. He then requested that he be allowed to take predigested bean flour again. Without making any other change in the diet, he did this, and gained one pound each week for two weeks (the bean flour being then flavored), and his appetite improved together with his gain. The conditions in this case are hardly worthy of special comment, though rather favoring the bean flour.

In another case, however, very remarkable results were obtained, and this case is sufficient to encourage the further use of the preparation in children past infancy.

CASE XXVIII.—A girl, aged two years, who in brief had the following history: She had been running down for a year; had had persistent digestive disturbance during this time, with constant diarrhoea and occasional vomiting, and nothing seemed to agree with her. She had constantly lost weight at the time when seen by Dr. Charles H. Schoff, of Media, who treated her with predigested bean flour. She had been for three months before this at Atlantic City, under the care of several skilful clinicians, and was then seen by Dr. J. P. Crozer Griffith, who tried a variety of diets without success. The child seemed entirely unable to take milk even when it was greatly diluted, and other liquids agreed but little better. She was then tried on semisolid and solid food, but grew decidedly worse. She was referred to Dr. Schoff at this time, and was then having from ten to fifteen bowel movements a day, which were loose and green. She was vomiting several times daily; was emaciated and extremely weak; her hands and feet were cold, and she was apparently in a desperate state. She weighed eighteen pounds. Several days of careful dieting and medication brought no improvement, and at our suggestion Dr. Schoff tried predigested bean-flour solution, alone, in small amounts. Finding that this did well it was rapidly increased, and the child was given eight ounces of 10 per cent. solution every three hours. Dr. Schoff states that within twenty-four hours the bowel movements were much reduced and much improved in appearance, and the vomit-



ing had stopped. Within a few days more the bowel movements were reduced to about three daily and the child's general condition was greatly improved, and after this there was continuous general advance in health and improvement of the digestive tract. In the first week a gain of slightly less than a pound was made; in the second week a similar gain; in the third week a little over two pounds; in the fourth week two pounds. At this time it was attempted to give the child a very small amount of milk with the bean flour, but it immediately disturbed the digestion. Two weeks later other foods were gradually added, and the child when last heard from had continued to gain and was to all appearances perfectly normal excepting for a tendency to intestinal disturbance from slight causes. This child objected to the taste of the bean flour at first, but took the subsequent feedings readily.

In this case the usefulness of the preparation probably depended upon the fact that it is extremely easy of digestion, has a high nutritive value for its bulk, and contains (that which most other very easily digested preparations do not) an amount of proteid that is entirely sufficient for the needs of the organism. In similar cases, even when much less severe, it would be worthy of trial. It would also be worthy of trial (if agreeably flavored) in cases of acute infectious diseases, particularly in typhoid fever, when there is difficulty in digesting the proper amount of milk. In these cases the addition of a small amount of this preparation would increase the nutritive value of the food, and would sometimes improve the digestion—if in no other way, through its action upon the curd of the milk. It has become the custom of one of us, in a hospital service in which large numbers of cases of typhoid fever are seen, to treat any digestive disturbance on exactly the principles that are used in the treatment of digestive disturbances in infants, reducing the fats or the proteids or both as seems wise, and frequently adding a cereal to prevent the formation of large, tough curds. The latter is a particularly useful procedure in a certain number of cases, and we have seen it rapidly control serious disturbance of digestion, with diarrhœa, distention, etc., in typhoid cases. Predigested bean flour in the form in which we use it has, as we could readily determine, the same influence upon the curd as barley-jelly and the like, and it has also another influence—it is necessary to add much more acid to milk to curdle it when predigested bean flour is present than when it is not. This is probably due to the acid combining with the proteid of the bean.

These clinical results seem to us on the whole to be decidedly favorable. It is to be remembered that all the infants treated were hospital babies, and that with one exception (the last St. Christopher's Hospital case) they had all been losing before the bean flour was started, or had at best merely maintained a very low weight. We would also have it especially noted that no change was

made in the diet excepting that a portion of what the infants had been getting immediately before was cast out, and in its place an equivalent, or usually very slightly less, value of bean flour was given. All the St. Christopher's Hospital cases, excepting the last, are of little importance, since all were in extremely bad condition when the bean flour was started, and only three of them got this preparation as long as a week. These three did a little better than they had done for some time before, though they all died. Of the cases treated elsewhere, three have been classed as unfavorable. The first of these was at the time probably not in condition to receive this or any other food, except the most dilute, and hence was certainly not a suitable case for trial of the food. In the second case there was a rapid gain at first, and then an acute illness which was not due to the diet. In the third case there was some gain, though on the whole the infant did not do well; but the milk mixture used was certainly very concentrated for an infant of the age and digestion of this one, and a lower modification might have done better. In none of these instances was there any actual evidence that the food did harm. The other infants all gained and all were continuously improving when they passed from observation, most of them having increased largely and rapidly in weight and strength and many of them having much improved digestions. Eleven out of fourteen infants, therefore, showed decided improvement, and most of them showed very striking improvement.

Atrophic infants, when treated in hospitals, certainly do not usually show so high a percentage of improvement and such large gains. Indeed, in our experience, and certainly in that of most other observers, such cases are, in hospitals, most unsatisfactory to treat, and usually show persistent downward progress. We think, therefore, that there is good reason to encourage a more extensive trial of the preparation.

There are, of course, several evident reasons why one may be doubtful whether the legume flour had any influence in these cases that was peculiar to itself. The readiest objection that could be raised we have already met—the improvement was certainly not due merely to increase in the amount of food, for the amount of bean flour was purposely kept only equal to or a very little below the amount of milk mixture that it displaced. Those who use very low modifications may consider that some of the infants, at least, had had too strong a milk mixture previously, and that the improvement was due to dilution of the milk. There may be some truth in this, for some of the milk mixture was displaced by the bean-flour solution, and there was, therefore, a little dilution of the milk, but if this is the explanation of the results it means that these babies digested and absorbed the bean-flour solution better than they did modified milk, for the food as a whole was not appreciably diluted, the bean flour, as stated, maintaining

the actual concentration of the total food at practically the previous point. Another possibility that might be suggested is that improvement did not occur because of any influence of bean flour as such, but merely because of its mechanical effect on the curd. This is almost certainly not the case, for most of the babies had already received either barley-water, barley-jelly, malted barley-jelly, predigested wheat flour, or arrowroot.

Three points are, however, subject to somewhat serious criticism. In the first place the number of cases is small, and a larger number may show that our results were due simply to chance good fortune. Again, our cases were necessarily under observation for but short periods, and longer observation is necessary before it can be stated whether infants can often be brought back to good health by this means. Further, we have suggested that the bean flour probably exercised a special influence directly upon metabolism; that is, that it did not act solely through its influence upon digestion, or through the fact that an increased amount of food was being absorbed by babies who had previously been unable to take enough. This we have not definitely proved, but in support of our suggestion we have the following facts: While it is true that in most instances the digestion was more or less decidedly improved under the use of bean-flour solution when there was previously distinct digestive disturbance, it is equally noteworthy that in a number of instances the digestion was but little disturbed beforehand. In most instances also the gain in weight and strength was almost immediate, and it was usually very rapid, while the digestion in repeated instances improved only much more gradually; so that it appeared in such cases that the improvement of digestion was a part of the general improvement rather than the cause of it. Further, and most important, there was in some instances little or no change in digestion, and yet very marked improvement occurred; for example, in the first two cases in which absorption was studied the bowel movements of the two periods remained about the same, and the figures show that the actual absorption was already good and practically did not change when bean flour was given, yet both infants gained nearly a pound in six days, and afterward continued to gain while they had previously been stationary. That this food is capable of causing much improvement of digestion was shown by a number of the cases, most strikingly by Dr. Schoff's very remarkable case in the two-year-old child, in which the result was probably due chiefly to the influence on digestion. Disturbance of digestion, however, does not constitute the whole of the pathology of infancy. In dealing with adults there is an increasing and proper conviction that a good deal more digestive disturbance than was once thought is dependent upon some general disorder of nutrition; that is, that the disorder of digestion is not the primary condition, but is itself a result of some other disease; and the fact that digestive dis-

turbance is of enormous importance in infancy and early childhood need not, as it often does, render obscure the similarly important fact that in not a few instances in infants also the most important disturbance is one of general nutritive processes rather than of the digestive organs.

In order to give satisfactory evidence that the successful results in our cases were due to a special influence of the bean flour, and, particularly, to a special influence of the bean proteid, we must, however, demonstrate that similar results cannot be obtained in a similar proportion of cases by means of predigested starches of other forms. To a limited extent we have given evidence of this in the cases so far studied. One infant had been on Keller's malt-soup, and also on malted barley-jelly, with no improvement; another infant was treated with predigested wheat flour with slight improvement, then became stationary, and immediately afterward gained rapidly, as long as it was under observation, when we used bean flour. The cases seen at St. Christopher's Hospital also favor somewhat the view that wheat flour produces less successful results than bean flour.

If legume flour has this special influence upon the metabolism of atrophic infants, we think it may most readily be thought that it is due to the effect of the nuclein, or possibly to other particular substances in the flour, but not to the mere gross quantity of proteid in it, for the actual amount of proteid absorbed, as seen in the experiments detailed, was almost the same when bean flour was being used and when it was not.

**SUMMARY.** Bean flour in which the starch is predigested by means of a diastatic ferment seems to be well digested and absorbed by infants and adults. An extremely concentrated food may be given in this way in fluid and partially digested form; a 20 per cent. solution, although fluid, is practically equivalent to beefsteak in nutritive value. Its influence upon the digestive tract in infants in the cases studied was usually distinctly favorable, and its influence upon metabolism in infants and adults is at least equal to that of milk. Of fifteen infants treated, one did not gain; one gained rapidly, but had an intercurrent illness and the flour was stopped; one gained nine ounces and then almost ceased to gain. The others gained as follows: one, fifteen ounces in six days; one, thirteen ounces in six days, both continuing after the bean flour gave out; one, one and a half pounds in sixteen days; one, one and a half pounds in twenty-three days; one, one and a half pounds in seventeen days; one, over two pounds in four days, and after readmission twelve ounces in eleven days; one, one and a half pounds in twenty days; one, twelve ounces in eleven days; one, four ounces in three days (then taken home); one, one pound in seven days; one, one pound in eight days; one, one and one-half pounds in three days. All these were atrophic infants that had previously been stationary or

losing. A child of two years that had had persistent and very dangerous disturbance of digestion with advanced malnutrition improved immediately, the digestive tract became nearly normal within a few days, and the child repeatedly gained over two pounds a week. The last-mentioned child took nothing but bean-flour solution; the infants took usually about  $2\frac{1}{2}$  per cent. of bean flour in milk modifications.

These results are certainly unusual. They need to be controlled in several ways before any definite conclusions can be drawn from them, but it seems possible that they were due to a special influence of the legume flour on metabolism, and, perhaps, to a particular influence of the nuclein contained in this flour upon the tissue-building processes.

One point that appears to be of some importance we have definitely determined: it is easily possible to administer in this way as much as 0.75 per cent. to 1.0 per cent. of proteid, a fact of decided consequence in those common cases in which it is difficult or impossible to administer a proper amount of milk proteid.

It is desirable to test this preparation further in older children and adults who are the subjects of malnutrition. This will necessitate, however, some method of preparing the bean-flour solution by which it can be pleasantly flavored, as when unflavored its taste prevents its use with older patients for any considerable period. Infants, however, take it readily in milk.

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### THREE CASES OF POISONING BY POTASSIUM CYANIDE.

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CASES of poisoning by cyanide of potassium are not frequent in this country, being met with more frequently in England, Germany, and France. The drug is usually taken with suicidal intent; thus, in 402 cases of cyanic poisoning collected by Witthaus<sup>1</sup> in 65.4 per cent. of cases the poison was taken for this purpose. Of this number cyanide of potassium was the drug used in 83 cases. Of the 256 suicides, but 43 were women, and of those who took cyanide of potassium 5 were relatives of photographers and 4 of platers. This fact is of interest, as the majority of cases reported occur among photographers, electroplaters, mirror-makers, chemists, and soldiers, their occupations rendering the procuring of the drug comparatively easy.

I am indebted to Dr. John D. Curran, of Binghamton, New

York, under whose observation the first case came, for permission to report it.

CASE I.—A. B., female, aged thirty-eight years, hair-dresser by occupation. Had been dyeing a patron's hair during the afternoon with a dye containing silver, thus discoloring her fingers. On her way home from work she entered a drug-store, asking for ammonia with which to remove the stains. The clerk gave her several large pieces of cyanide of potassium, telling her that "this is better than ammonia," advising her to moisten her fingers and rub them with the cyanide of potassium, but failing, either through ignorance or carelessness, to inform her of the poisonous properties of the drug. At ten o'clock that evening she entered her bath-room, a small room (dimensions about 6 x 8 feet), imperfectly ventilated by one small window opening into an air shaft. Selecting a piece of cyanide of potassium about the size of a hickory-nut, she rubbed it vigorously on her fingers and hands, removing the stain. This took about five or ten minutes, at the end of which time, *and before she had an opportunity of washing her hands*, she was suddenly attacked with vertigo, felt faint, "everything turned black before her," and she experienced much difficulty in breathing. Her husband, in an adjoining room, heard her scream, and, rushing in, found her unconscious. He carried her into the fresh air and succeeded in a few minutes in restoring her to consciousness, she then taking about two ounces of whiskey. She improved rapidly, and soon was able to walk up stairs and go to bed. At 11.30 P.M. she became much worse, vomited freely, and Dr. Curran was called. He found her with her lips, fingers, and extremities deeply cyanosed. She was in a condition of shock, as evidenced by her subnormal temperature, cold perspiration, rapid, weak heart action, and sighing respiration. Under repeated hypodermic injections of strychnine sulphate,  $\frac{1}{30}$  grain, and atropine sulphate,  $\frac{1}{100}$  grain, with the application of external heat, she improved for about one and one-half hours, when she became restless, active, and tossed her head from side to side. This condition of motor activity was probably due to the action of the strychnine, which had been given freely during the period of collapse. She was readily quieted by the administration of morphine sulphate,  $\frac{1}{8}$  grain, given hypodermically, and fell into a quiet sleep, from which she awoke the next morning weak and somewhat prostrated. During the following day she was nauseated, her heart action rapid and weak, and she continued to give some evidences of shock. She made a rapid and uneventful recovery, being up and about the third day.

The following cases came under my own observation while resident physician in the Pennsylvania Hospital, Philadelphia:

CASE II.—George R., aged thirty-five years, mirror-maker, admitted to the Pennsylvania Hospital February 8, 1901, with the following history:

About fifteen minutes before his admission to the hospital he entered a saloon, sat down, and called for a drink of whiskey. Upon receiving the liquor he placed a small quantity of a white substance into it and a few minutes later picked up his glass and drank the contents. He almost immediately fell forward on his face, unconscious, without uttering a sound. He was hurried to the hospital, where upon admission his condition was as follows: Completely insensible; face cyanosed. Respiration somewhat jerky in character, twenty per minute. Jaws clenched, requiring a gag to open them. Some mucus in mouth. Characteristic odor of bitter almonds on breath. Pulse weak and small. Eyelids closed; eyes fixed; pupils dilated, equal, did not react to light or accommodation; conjunctival reflexes absent. No escape of urine or feces.

Patient was immediately given a hypodermic injection of strychnine sulphate,  $\frac{1}{10}$  grain; his jaws separated, the stomach tube introduced, and his stomach thoroughly washed out with warm water. Sylvester's method of artificial respiration was instituted. Despite this the cyanosis increased rapidly, and he died eight minutes after admission. A considerable quantity of cyanide of potassium, properly labelled, was found in his pocket.

The post-mortem examination made by the coroner's physician, Dr. Wadsworth (to whom I am indebted for the findings), showed the heart to be normal, excepting for a considerable deposit of fat; the lungs were congested. The stomach was empty; the mucous membrane much inflamed, especially toward the pyloric end. The liver and kidneys were slightly engorged.

CASE III.—X., male, aged about forty years, was found dead in bed in a hotel. He was last seen alive about eight hours before his body was discovered.

The post-mortem examination made by the coroner's physician, Dr. Morton (who kindly furnished me with the findings of the examination), showed results quite similar to those found in Case II. The heart was normal, excepting for beginning atheroma in the aorta. The lungs were much congested and dark in color. The larynx was also much congested. The mucous membrane of the stomach was greatly inflamed, especially at the pyloric end. The odor of hydrocyanic acid was noticed immediately upon opening the stomach. The liver was engorged, as were also the kidneys. The mucous membrane of the bladder was not inflamed.

Dr. Curran's case (Case I.) is of great interest, as there was apparently poisoning by cyanide of potassium by two methods in the one case. The unconsciousness and vertigo, which the patient first experienced, were unquestionably caused by the inhalation of the drug in a small, poorly ventilated room. The period of shock, occurring an hour and one-half later, was undoubtedly due to the absorption of the drug through the skin, it being recalled

that after removing the silver stains from her hands with the cyanide, the patient had no opportunity of washing her hands, falling unconscious before she could do so. That poisoning by these two methods may, and does, occur is proven by cases reported by Souwers<sup>2</sup> and by a writer in the *British and Foreign Med.-Chir. Review*.<sup>3</sup>

The minimum lethal dose of cyanide of potassium varies, according to the different authorities, but is generally fixed at from 2 to 5 grains, Bennett<sup>4</sup> reporting two cases with fatal results after taking 2 grains and  $4\frac{1}{2}$  grains, respectively. Death does not occur as rapidly in cases of poisoning by potassium cyanide as in cases of hydrocyanic acid poisoning, usually not taking place for from fifteen minutes to an hour after the ingestion of the drug. Cases are reported, however, in which death has taken place in less than ten minutes, Casper-Liman<sup>5</sup> reporting a case in which the drug was taken with suicidal intent by a young woman twenty years of age, death occurring "immediately." Valcourt<sup>6</sup> and Haskins<sup>7</sup> mention cases in which death resulted in two and five minutes, respectively. The mortality in cases of cyanic poisoning is high, Witthaus<sup>1</sup> stating that in 455 cases, 382, or 84 per cent., died. Death in these cases is due to paralysis of the respiratory centre, although it would appear that in some cases it is caused by the depressant action of the drug upon the heart itself.

That recovery frequently takes place, even after the ingestion of large doses, is shown by cases reported by Higgins,<sup>8</sup> Wiglesworth,<sup>9</sup> Stevenson,<sup>10</sup> Quintin,<sup>11</sup> Brockett,<sup>12</sup> and Gillibrand,<sup>13</sup> in which from  $19\frac{1}{2}$  grains to 50 grains of cyanide of potassium have been taken, the patient in each instance recovering. While death takes place more slowly in fatal cases of cyanide of potassium poisoning than in fatal cases of hydrocyanic acid poisoning, recovery is more delayed in these cases than in those of hydrocyanic acid poisoning. Unconsciousness generally persists from two hours to six or eight hours, Dobson,<sup>14</sup> Quintin,<sup>11</sup> and others reporting cases in which the period of unconsciousness extended over this length of time, and one remarkable case is reported<sup>15</sup> in which the unconsciousness persisted for three days, the patient not being discharged from the hospital for ten days. In the other cases cited the patients have usually been discharged in from three to four days.

Autopsy has usually shown the left ventricle of the heart empty and firmly contracted, the right containing uncoagulated blood. The stomach is frequently found much inflamed, especially toward the pyloric end. The lips, mouth, and stomach at times show evidences of corrosive poisoning, probably due to the carbonate of potassium used in the manufacture of the cyanide of potassium.

The most important factor in the treatment of cases of cyanic poisoning is the promptness with which it is instituted. Immediate evacuation of the stomach and intestinal canal, the administration



of cardiac and respiratory stimulants, artificial respiration, friction of the extremities, and cold affusions to the spine, with the patient in a warm bath, or the use of the alternate hot and cold douche to the spine, offer the best results. Various drugs have been suggested as additions to water in washing out the stomach: hydrogen peroxide; potassium permanganate; ferric and ferrous salts in combination; carbonate of potash in solution or in combination with sulphate of iron and ether. Of these probably the best is the permanganate of potassium, the use of which is recommended by Kossa<sup>16</sup> and other writers. Witherstine<sup>17</sup> calls attention to the article of Heim,<sup>18</sup> in which the author states that "morphine seems to be the antidote to cyanide of potassium, and vice versa."

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## EVENTRATION OF THE DIAPHRAGM, WITH A REPORT OF A CASE.

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EVENTRATION of the diaphragm has been known ever since J. L. Petit reported and named a case in 1790. It may be described as an abnormally high position of the left half of the diaphragm, with dislocation upward of the abdominal viscera, particularly the stomach, on the left side; hypoplasia of the left lung, and displacement of the heart to the right. It gives rise to physical signs closely resembling those of diaphragmatic hernia. Its proper

classification has been a matter of considerable difficulty. The greater number of writers (Laacher, Thoma, Leichtenstein) include it among the forms of diaphragmatic hernia, regarding the distended diaphragm reaching high into the abdominal cavity as a part of the hernial sac, the other layers being the pleura above and the peritoneum below. Others (Reinhold) consider the chief feature the hypoplasia of the lung. A third group (Crispino) regards such cases as instances of dextrocardia, a fourth group (Doering) as primary defects of the diaphragm, and a fifth group (Cruveilhier, Glaser) as possibly acquired lesions.

The following case was observed at the Philadelphia Hospital in the service of Professor James Tyson, to whom we desire to express our thanks for permission to publish it:

H. H., white, aged twenty years, a farmer.

*Family History.* His father died at the age of seventy; his mother was living. She was said to be nervous and to have had "spells" until she was twenty years old. Five half-brothers and three half-sisters were all said to be nervous.

*Present History.* Patient had one convulsion in infancy, a second at the age of fifteen years, and since then they had occurred about once a week; otherwise he had been healthy. The convulsions appear to have been typical epileptic attacks commencing with nausea and vertigo, and followed by unconsciousness, during which the patient fell to the ground, but rarely injured himself. Sometimes he bit his tongue. After the attacks he felt exhausted, had headache, and ordinarily slept for two or three hours. When he awoke he complained of peculiar dreams. He was admitted to the ward for nervous diseases in the service of Dr. Charles W. Burr, where it was noted that he was well developed, well nourished; that the pupils were equal and reacted normally; that there were no pareses, but that the tongue showed a constant tremor. It was also noted that there was hyperresonance over the whole left side of the chest; that the area of cardiac dulness was absent; that the apex beat could be felt to the right of the sternum; that the other organs were normal in position. Three days after admission he began to complain of abdominal pain; he developed fever, and had an enlarged spleen, and three days later rose-colored spots appeared upon the abdomen. He was therefore transferred to the medical ward. Upon admission the following notes were made:

"The left side appears to be larger than the right; no cardiac impulse is visible on palpation to the left of the sternum, but there is distinct impulse visible in the third, fourth, and fifth interspaces to the right of the sternum. The percussion note over the left side is tympanitic below and resonant above the second interspace. The tympanitic note extends from the midsternal line to the mid-axillary line. On the right side there is a little fulness in the upper portion of the chest, and tenderness as far down as the second rib.

The percussion note is resonant, but not tympanitic. In the third, fourth, and fifth interspaces there is an area of dulness which is continuous with the liver dulness, extending from the midsternal to the parasternal line. The respiratory sounds are absent on the left side below the level of the fourth rib anteriorly, and below the level of the third rib laterally. Below this point a considerable amount of gurgling and bubbling can usually be heard. Above the fourth rib the respiratory sounds are vesicular, but harsh. The heart sounds are faint on the left side and loud on the right side, and the second sound is distinctly accentuated. The patient shows general cyanosis."

*History in the Medical Ward.* One week before admission, after exposure, the patient had a chill, accompanied by vomiting. Since then he had been feverish and chilly, and had had several attacks of epistaxis, and cough with blood-streaked expectoration. There had been some pain in the abdomen.

*April 10, 1902,* the following notes were made: "The tongue is moist and tremulous; the pulse rapid, weak, and regular. There is bulging in the intercostal spaces on the left side, and a visible cardiac impulse in the third, fourth, and fifth interspaces just to the right of the sternum. Percussion resonance is normal on the left side as far as the second rib; below this there is distinct tympany extending from the midsternal to the midaxillary line. If the patient inspires deeply the upper border of the tympanitic area descends about an inch. There is a slight prominence in the right infraclavicular space which is tender. The area of cardiac dulness extends one inch to the right of the sternum, and from the lower border of the third rib to the hepatic dulness. The percussion note over the rest of the right side is clear. The breath sounds are very faint on the left side below the third rib. Over the tympanitic area bubbling, gurgling, and splashing are heard. When the patient swallows water and the stethoscope is placed over the tympanitic area the gurgling sounds are clearly transmitted to the ear. The heart sounds are faint on the left side, but loud on the right, and there is accentuation of the second sound. In the lower part of the left side anteriorly there is a to-and-fro sound resembling friction rub. When the patient is placed upon the right side the area of tympany extends as far back as the posterior axillary line. There is dulness along the left border of the sternum. Posteriorly the breath sounds can be heard indistinctly at the base of the left chest. The coin test is not obtained."

The following extracts from the notes relate most intimately to the physical condition:

*April 11th.* Two exploratory punctures were made, but were entirely negative. It felt as though the needle were in a hollow cavity. The course of the disease has been steadily progressive. From time to time the patient has had severe hemorrhage from

the bowels; the diazo and Widal reactions have been positive, and the eruption is typical. The respirations are never very rapid.

14th. There seems to be a slight but appreciable movement of the area of dulness to the right of the sternum, farther to the right and slightly upward.

15th. Auscultatory percussion over the tympanic area indicates that it is apparently continuous with the abdominal cavity. When the stethoscope is placed over this area, and the abdomen tapped, the sound is clearly transmitted, unless the tapping is made over the area of liver dulness, over the right lung, or above the third rib.

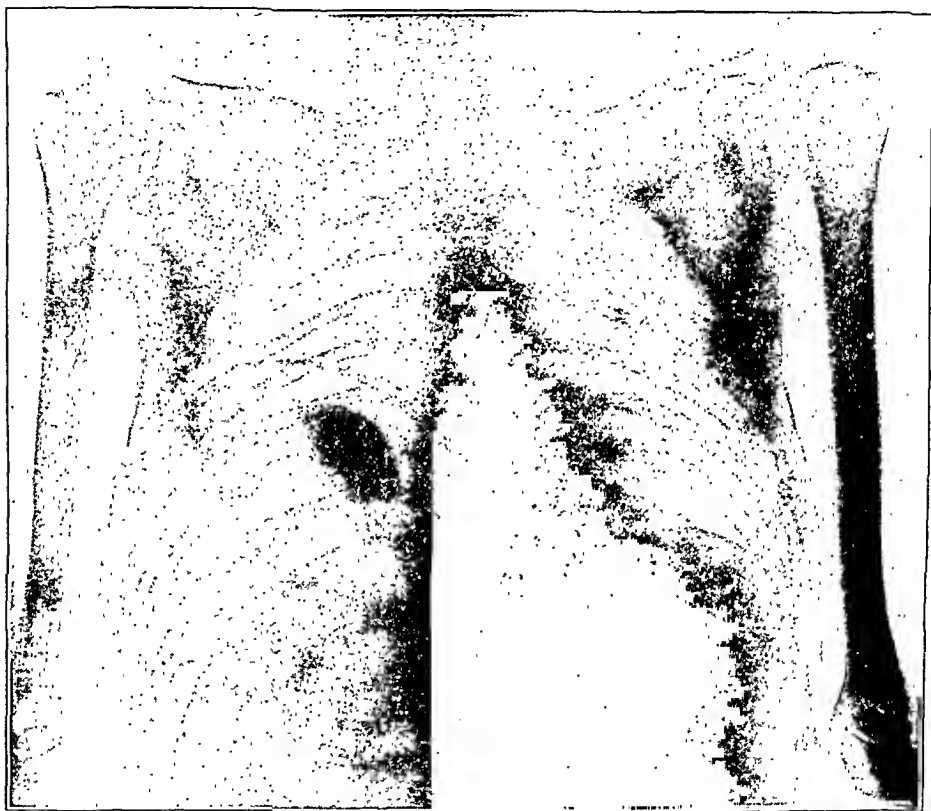
25th. The patient has had an epileptic attack. For the preceding two days he has had dyspnœa.

After this date he continued to grow worse, extensive and uncontrollable bed-sores developed, he expectorated large quantities of rusty sputum, the respiration, increased in frequency, and the heart was apparently displaced slightly farther to the right. The area of tympany remained unchanged. Posteriorly there was a slight area of dulness extending from the angle of the scapula to the base of the lung. This area moved slightly when the patient was rolled upon the right side. Over it the breath sounds were harsher than over the tympanic area. The pulse became weaker, and at 8.45 on the morning of April 30, 1902, the patient died. The blood count was made only once, when there were 4000 leukocytes. Throughout the course of the disease he had suffered from excessive thirst. Litten's phenomenon was never satisfactorily obtained, partly on account of the serious condition of the patient.

Immediately after death Dr. G. E. Pfahler took a skiagram of the thorax and abdomen of the patient. This was not developed until after the autopsy, but would alone have rendered the nature of the condition perfectly clear.

The diagnosis of this condition presented many difficulties, chiefly on account of our unfamiliarity with the condition. At various times we suspected pneumothorax, diaphragmatic hernia, pulmonary cavity, and high position of the diaphragm. In a subsequent study of the literature it appeared that we should also have considered subdiaphragmatic pyopneumothorax and unilateral paralysis of the phrenic nerve. In favor of *pneumothorax* was the movable dulness on the left side posteriorly. This, however, was always doubtful, and the condition appeared to be excluded by the absence of dyspnœa, the equal expansion of the two sides during respiration, the negative coin test, the movement of the upper border of the tympanic area during respiration, failure of the supposed fluid to increase during the course of the disease, and the absence of leukocytosis. A tympanic note, moreover, is rather uncommon over a pneumothorax. The diagnosis of *diaphragmatic hernia* was concurred in by Dr. Riesman, who also saw the case.

In favor of this was the area of tympany in the lower portion of the left chest, the dislocation of the heart to the right, the loud gurgling heard in the tympanitic area when the patient swallowed water, and the excessive thirst. Against it was the absence of dyspnœa, the equal expansion of the two sides, the area of dulness posteriorly, and particularly the distinct respiratory movement of the upper border of the tympany. Cavity in the lower portion



The skiagram was taken with the patient's back to the plate. It is, therefore, as if the patient were standing with his back toward the spectator. On the right side is seen the heart, and below that the convex upper surface of the liver, indicating the position of the right half of the diaphragm. On the left side there is, next to the spinal column, a narrow band of shadow indicating the left border of the heart. Then, arising from the vertebral end of the seventh rib, arching to the left and upward as far as the fifth rib and axillary line there is a convex shadow indicating the position of the left half of the diaphragm. The large dark mass just below this was found at the autopsy to be a huge coagulum of milk lying in the stomach. Below this the attachment of the diaphragm can be seen, represented by a broader line convex on the upper surface, and below this and to the left of the vertebral column a lighter shadow, indicating the position of the spleen. (The skiagram was taken by Dr. G. E. Pfahler.)

of the left lung was also suggested, but there was neither bronchophony nor pectoriloquy over the tympanitic area, no paroxysms of profuse expectoration, and in cavity formation dislocation of the heart, excepting toward the cavity, is exceedingly uncommon.

High position of the diaphragm accounted satisfactorily for the dislocation of the heart, the respiratory movement of the upper border of the tympany, and for the gurgling heard over the tympanitic area, particularly if the water was swallowed during auscultation. We did not understand why there should have been a supposed movable dulness posteriorly, nor could we account for the friction sound occasionally heard in the fifth interspace near the left midaxillary line. Nor was there any obvious cause why the diaphragm and with it the abdominal viscera should have been displaced. It was therefore supposed that it might be congenital, possibly one of the forms of physical anomaly sometimes associated with epilepsy. Hypoplasia of the left lung was not suspected during the patient's life.

The autopsy was made by Dr. Prince five hours after the patient had died. The pathological diagnosis was: Congenital malformation and hypoplasia of the left lung, compensatory distention of the left half of the diaphragm, splenic tumor with septic infarction, enlargement of the liver, acute nephritis, and enteric fever. The most important parts of the notes are as follows:

There was a large bed-sore over the sacrum and one over the seventh cervical vertebra; also beginning bed-sores on each heel. Abdominal cavity: The lower edge of the stomach could be seen just beneath the costal border; its position was almost vertical. The spleen was greatly enlarged; its lower border was at the level of the border of the ribs anteriorly. The left kidney was in its normal position. The tail of the pancreas pointed vertically upward along the left side of the sternum. The diaphragm turned sharply upward just behind the xiphoid cartilage, and on the left side reached to the third intercostal space. On the right side it reached to the fifth rib. Thoracic cavity: The left pleural cavity was abnormally small, the dome of the diaphragm reaching high into the chest. The heart was displaced toward the right and extended 5 cm. to the right of the midsternal line, and from the third to the sixth ribs. The left lung was abnormally small; the length of the outer edge was 16 cm. and of the anterior edge 13 cm. Its greatest width was 18 cm. The lower lobe was imperfectly divided into three small lobes; there were some areas of atelectasis posteriorly and slight emphysema anteriorly. The right lung was apparently normal in size. The middle lobe was imperfectly separated from the upper. It was slightly emphysematous and showed a few small areas of atelectasis. The spleen measured 15 x 6 cm. The substance was firm; there was a large, softened, anæmic infarct on the greater convexity, and a second somewhat smaller infarct a short distance from this. It was placed close to the spinal column, with its long axis vertical and extending upward to the level of the sixth dorsal vertebra. Microscopically the diaphragm contained muscular fibres.

The physical signs were satisfactorily explained by the autopsy. The left lung was less than half its normal size, and the small areas of atelectasis at the surface did not permit, in the presence of emphysema of the other portion, of the supposition that it had ever been compressed. It must, therefore, have been hypoplastic, and coincidently with this hypoplasia the diaphragm had risen to fill the left pleural cavity. The diaphragm was moderately thin, but microscopically was found to contain a fair amount of muscular tissue, which accounted satisfactorily for the respiratory movement. The area of dulness to the left of the sternum posteriorly was evidently due to the greatly enlarged spleen which was found in this situation, and it is entirely possible that in rolling the patient from side to side this large and heavy organ may have shifted enough in position to give the impression of movable dulness. It is also possible that the rubbing of the spleen against the wall of the abdomen gave rise to the friction sound. No other cause was found at the autopsy.

The condition was unquestionably congenital, for, in addition to the peculiar deformity of the left lung, it seems likely that the dislocation of the tail of the pancreas upward must have occurred during embryonal existence.

The following list of cases of this condition is as complete as we could make it. Unfortunately it was impossible to verify all of the references, and some of the cases are so incompletely reported in abstract that their nature is doubtful:

CASE I.—Jean Louis Petit mentions the case of a woman who had had attacks of asthma for some years, which were usually relieved by eating. She died of inflammation of the stomach (peritonitis?), and at the autopsy a tumor the size of a small gourd was found projecting into the left pleural cavity. It contained the stomach, colon, and great omentum. Its wall was composed of the pleura, the peritoneum, and the diaphragm. He describes it as a form of diaphragmatic hernia.

CASE II.—Lawrence reports the results of an autopsy in which the liver was found displaced in the right lumbar region; the diaphragm on the left side reached to the second rib, forming a sac which contained a greatly dilated stomach. The left lung was reduced to the size of a fist, and the left half of the diaphragm formed a thin, flaccid septum which was continuous with the muscle on the opposite side. The right half was normal. The position of the heart is not mentioned.

Laacher, in his article, mentions the two following cases:

CASE III.—Pyl describes the findings of an autopsy upon a newborn infant. On the left side the diaphragm was thin and dilated as if it were a hernial sac. This sac contained the stomach, spleen, ileum, and the curve of the colon. The heart was pushed to the right. He regards it as a *hernia vera*.

CASE IV.—Meckel describes a female foetus, the left side of whose diaphragm was dilated into a sac containing the stomach, the jejunoleum, the cæcum, the colon, and the spleen.

CASE V.—Froriep mentions the case of a girl who died at the age of nineteen years. She often had dyspnœa and vomiting and other digestive disturbances. From the fourteenth year she had had obstinate constipation. At the autopsy the left half of the diaphragm appeared as a sac reaching upward into the pleural cavity, and containing the stomach. The heart was pushed considerably to the right. The diaphragm was abnormally thin, and in the neighborhood of the mediastinum was transformed into transparent cellular tissue. This abnormal thinness appeared to be congenital, for no other cause, such as inflammation of the diaphragm or of the diaphragmatic pleura, existed.

CASE VI.—Marsh reports the case of a man who had a severe shock followed by a sense of something giving way, and then cough, dyspnœa, and pain in the left side of the chest. At the autopsy the left half of the diaphragm arched into the left pleural cavity as high as the level of the left intercostal space. The stomach was concealed beneath the ribs. The liver lay below and in front of it. The right half of the diaphragm was normal. The left half contained a few muscular fibres; the left crus was about half the size of the other. The lungs showed the changes of acute croupous pneumonia, but were otherwise normal; their size is not mentioned.

CASE VII.—Thoma describes the findings at the autopsy of a man of seventy-five years who had died of peritonitis. The diaphragm reached to the fifth rib on the right side and to the third interspace on the left side. The left half formed a large sac containing the stomach, spleen, the left lobe of the liver, and part of the colon, all of which were displaced upward. The apex of the heart was in the median line just above the xiphoid cartilage. The upper lobe of the left lung was large and extended far to the right; the lower lobe was very small, so that the whole lung was shorter. The right lung was deeply grooved on the anterior surface to receive the heart. The spleen was moderately and the stomach greatly enlarged. Thoma naturally regards the condition as congenital, particularly as other forms of congenital hernia were present.

CASE VIII.—Crispino reports, as an instance of congenital dextrocardia, the case of a woman fifty-five years of age. There was no deformity of the chest. There was a small left inguinal hernia. The apex of the heart could be felt in the fifth interspace in the right anterior axillary line; the heart dulness commenced at a point above the fourth rib and extended from the right border of the sternum to a line between the right nipple line and the right anterior axillary line. The lungs were entirely negative. Auscultation of the heart revealed only slight arrhythmia. He expressly



states that the spleen, stomach, liver, etc., were in their normal positions. But he then describes a radiograph which showed that the heart was greatly displaced to the right, and that the left half of the diaphragm was higher than the right, the difference being about four inches. It moved easily and synchronously with the heart. The left lung appeared to be short, but very broad.

CASE IX.—Kronig reported very briefly before the Berlin Medical Society, as an instance of dextrocardia, the case of a man, forty-eight years of age, who died of pneumonia, and in whom, before death, a diagnosis of dextrocardia had been made. At the autopsy the heart was found dislocated to the right, but not otherwise anomalous. The left lung was very broad, and the relation of the lobes was altered so that the upper lobe lay directly in front of the lower.

CASE X.—Tennant reports the case of a man of sixty years who had had syphilis and psoriasis, and died as the result of double pneumonia. There was nothing in his clinical history to indicate disease of the gastrointestinal tract, and apparently nothing unusual had been discovered in the physical signs. The condition was found during dissection. There was no obvious external deformity excepting large bilateral inguinal hernias, which were not congenital. On the right the diaphragm extended to the fourth interspace; on the left the anterior third of the diaphragm was normal, then it bent sharply upward, forming an edge from the tenth rib to the central tendon, and a pouch that extended to the second interspace. This contained a distended stomach and coils of the transverse colon, which was fifty-five inches long. The membrane forming the pouch was thin and translucent, and contained only a few muscular fibres examined macroscopically. The apex of the heart was three inches to the right and one and a half inches to the right of the median line; the base was normal. The lungs were also normal and equal in size. The left phrenic nerve did not show any obvious degeneration. Tennant believes that the condition must either have been congenital or acquired as a result of the degeneration of the muscle of the diaphragm or the terminations of the phrenic nerve.

CASE XI.—Doering reports the case of a man of sixty years who had always performed severe manual labor. His thorax was slightly barrel-shaped but symmetrical, and there was possibly a slight diminution of the respiratory excursion on the left side posteriorly. Otherwise it was normal. Litten's phenomenon could not be satisfactorily determined. Percussion of the left side anteriorly showed slight impairment of resonance as far as the third rib; below this point there was a loud tympanitic note. Posteriorly the area of tympany commenced at the level of the fourth spine of the vertebra. On the right side percussion was entirely normal. The cardiac pulsation could be seen and felt in the fourth inter-

space, a finger's breadth to the inner side of the right nipple line. The dulness extended from one finger's breadth to the left of the left border of the sternum as far as the right nipple line, to the level of the third rib and the liver. Auscultation showed vesicular respiration at the apex of the left lung, loud intestinal gurgling over the tympanitic area, normal vesicular respiration over the right lung, and an accentuated pulmonic second. A diagnosis was made of dislocation of the heart and retraction of the left lung. At the autopsy the diaphragm was found reaching to the sixth rib on the right side, then bending sharply upward at the suspensory ligament of the liver, and forming a large sac the apex of which reached to the upper border of the third rib. The heart was entirely dislocated to the right, but was in itself normal. There were no pleural or pericardial adhesions. The lung consisted of three lobes. The left lung was small, measuring 14 cm. vertically, 12 cm. in breadth, and 6 cm. in length. The tissue was normal excepting a slight pigmented induration of parts of the middle and lower lobes. The right bronchus was larger than the left. There were no bronchiectases. The sac formed by the diaphragm contained portions of the stomach and colon and a large mass of intestinal loops. The spleen was small and in its normal position. The microscopic examination of the diaphragm showed that it consisted of three layers, one of the pleura, another of the true diaphragm, and between them a layer of laminated connective tissue. The muscular fibres were greatly diminished, and in the upper third of the sac were entirely absent. The left lung was normal.

CASE XII.—In 1901 Widenmann reported as an example of diaphragmatic hernia diagnosed during life the case of a man, forty-eight years of age, who had had four attacks of pleurisy. The last attack had commenced with profuse hemorrhage from the stomach. He was transferred to the hospital, where it was found that the left thorax was slightly prominent above and slightly retracted below. The expansion was almost equal. On the left side from the second rib to the fourth rib there was a hyperresonant note, and from the fourth rib downward tympany. Posteriorly there was loud tympany from the angle of the scapula to the level of the ninth spinous process, and below this dulness which continued to the upper border of the spleen. In the tympanitic area the breath sounds were practically absent, and on this account the intestinal gurgling could clearly be heard. Hippocratic succussion could be obtained after taking food. The heart was dislocated to the right; the area of dulness changed considerably with the position. The stomach contents were normal. When the stomach was distended there was no prominence in the left hypochondriac region; the area of tympany rose one interspace higher in the left chest. In order to confirm the diagnosis the patient was studied by the aid of the Roentgen rays, and a large clear space seen in the

lower border of the left thorax, bounded above by a line convex upwardly. On the first examination this moved with respiration, and a diagnosis of high position of the left diaphragm was made.

Later a transverse line below the clear area could be seen moving with the respiratory excursion, and a diagnosis was made of diaphragmatic hernia, the supposition being that the opening was in the posterior portion of the diaphragm, and that the left lobe of the liver had also passed through it, accounting for the area of dulness posteriorly. Notes taken twenty-six years before in the military hospital revealed practically the same condition. A year later Glaser reported the same case. The physical signs were practically the same. Litten's phenomenon could not be observed. If the stomach were filled with water, dulness appeared in the lower portion of the tympanitic area. The patient again had hæmatemesis, and incarceration of diaphragmatic hernia was diagnosed. An operation was performed, at which high position of the diaphragm was discovered. The spleen was dislocated upward, lying to the left and back of the fundus. The patient recovered from the operation, but a year later died from carcinoma of the tongue. At the autopsy the right apex of the diaphragm was found at the lower border of the fifth rib; the left apex at the level of the third interspace. The left half of the diaphragm contained the stomach and some intestinal loops. When the stomach was inflated the apex of the diaphragm on the left side rose to the level of the second interspace. The colon, duodenum, liver, and kidneys were normal in position; the spleen was dislocated upward; the heart was to the right. The left lung consisted of two lobes, the upper covering the lower. Benda examined the diaphragm and found what was apparently a fatty degeneration of the muscular fibres. Fraenkel, in whose service the case occurred, therefore regards it as an acquired high position of the diaphragm caused by a pseudohypertrophic lipomatosis of the diaphragmatic muscle.

In view of Widenmann's discovery of the record that showed that at the age of twenty-two years practically the same condition existed, the disease must have commenced in early life. Somewhat similar cases, both as regards the physical signs and the results of Roentgen examination, have been reported by Hirsch and Strüpler. Both have been diagnosed as diaphragmatic hernias, but it is entirely possible that they may really have been cases of eventration of the diaphragm.

In addition to these cases there are several other doubtful cases in the literature: 1 by C. J. Clark, in which it is not clear whether the condition was congenital or acquired; 1 by Abercrombie, 1 by Barlow, and 1 by Fitzgerald and Ernst. The

data are insufficient, and therefore it is not possible to include these cases.

Summarizing these 13 cases we find that 1 was a foetus; 1 a newborn infant. In 8 the age is given and ranged from nineteen to seventy-five years; in 3 it is merely stated that they were adults; 4 were females, 7 were males, and in 2 the sex was not given.

The clinical symptoms were various. In 1 there was asthma relieved by eating; another, a girl of nineteen, had suffered from vomiting and constipation; a third, a man of fifty, had had a number of attacks of hæmatemesis and symptoms of incarceration of a diaphragmatic hernia for which operation was performed. One patient had inguinal hernia, another bilateral inguinal hernia, and 1 suffered from epilepsy. In 2 cases evidences of peritonitis were found at the autopsy. One died of pneumonia, 1 of typhoid fever, and 1 of carcinoma of the tongue.

In 12 of these cases autopsies have been obtained; 1, the case of Crispino, is still alive, but the diagnosis appears to be established by the radiogram.

In 8 of the 12 cases the diagnosis was not suspected. In 1 a diagnosis of dextrocardia had been made during life, and in 3 the diagnosis was made with a reasonable certainty during life, Doering diagnosing high position of the diaphragm with retraction of the left lung, Glaser having established the diagnosis at an exploratory operation, and in our case the diagnosis of high position of the diaphragm having been made.

The condition of the lungs is mentioned in 8 cases. In 2 of these it is stated that they were normal, and in 1 particularly that they were of the same size. In 6 cases they were abnormal. Twice three lobes were present, and the lung was small, and in the remaining 4 cases the upper lobe was relatively much larger than the lower lobe, and its position in relation to it was somewhat anomalous.

The only important conclusion to be deduced from these figures is that eventration of the diaphragm does not interfere with the duration of life, nor does it necessarily produce clinical symptoms.

With this scanty material it would not be justifiable to attempt to draw any very definite conclusions were it not for the fact that all the cases exhibit a very remarkable similarity; indeed, with unessential variations, the description of the autopsy in one case might readily be used for all the others.

Regarding the nature of the condition there is some dispute. Cruveilhier intimates, but does not explicitly state, that in the case of Petit, which he studied, it may have been acquired. The evidence for this was in part the coexistence of peritonitis, but subsequent authors—with, I believe, the exception of Glaser, who derived his views from Fraenkel and Benda—have been inclined to regard it invariably as congenital. In favor of this is the fact

that 2 cases have been recorded occurring in newborn children, as well as the existence in several cases of distinct anomalies of the left lung and the presence in 2 cases of other forms of hernia. There is more difference of opinion as to how the lesion actually occurs. Thoma believes that the lung is chiefly at fault. He urges that weakness of the left side of the diaphragm cannot account for it, as in the foetus the liver protects both sides. There is a greater tendency on the part of the left lung to congenital malformation in the proportion, he finds, of 49 to 8. He suggests that it is not impossible that eventration might occur on the right side, although hitherto no such case has been recorded. The arguments in favor of this view may be summarized as follows: First, the occurrence of congenital anomalies in the lung; second, the presence of muscular fibres in the diaphragm in several cases examined microscopically; third, the absence of anomalies in the great vessels arising from the heart. The mechanism is, of course, obvious. When the lung is too small the diaphragm rises to fill the space in the pleural cavity, dragging the intestinal contents with it.

The theory that the primary lesion is a congenital deficiency of the muscles of one side of the abdomen has been supported chiefly by Doering. In favor of his view he urges the marked deficiency in the muscular tissue of the affected side of the diaphragm, which has been found in all cases examined microscopically, and the symmetrical condition of the thorax. The mechanism is that the congenitally weak diaphragm fails to expand the lung, which remains atelectatic, and therefore the diaphragm assumes the high position, dragging the viscera with it. Against this view is, of course, the existence of anomalies in the lung; the fact that the lungs have never been found to be atelectatic; and, I believe, the invariable presence of dextrocardia. Glaser suggests as an explanation of his own case that there occurred a dystrophy of one-half of the muscle of the diaphragm, causing it to become weakened and to rise in the thorax as a result of the traction of the lung.

Tennant suggests that in his case there may have been a degenerative condition either of the left half of the diaphragm or of the terminals of the phrenic nerve. It does not appear that microscopic examination was made for the purpose of determining this important point. It is not an exaggeration of a normal condition, for Engel has proven that the diaphragm is normally higher on the right side.

There are, I think, certain points in this condition which require more careful consideration. The symmetrical thorax early attracted attention. Neisser believes that it is due merely to the greater compensation that can occur in the intrathoracic viscera in early childhood, and particularly to the absence of adhesions between

the serous membranes. Doering implies that it is due to the tendency of the skeleton to develop symmetrically when there is no hindrance placed upon it. These views are practically identical. The fact that the diaphragm on the left side is thin and contains few muscular fibres is to my mind of considerable importance. If the primary lesion were merely a hypoplasia of the lung we should expect some evidence of hypertrophy of the muscular tissue as a result of the additional effort to which it was subjected. Such evidence is entirely lacking; indeed, in one case it was noted that even the pillars of the diaphragm were diminished in size. The dextrocardia hardly accords with the theory of primary hypoplasia of the lung. Assuming that the lung was too small, the natural effect of the tug of the diaphragm would be to displace the heart farther to the left. This is not merely a theoretical consideration. Cases have actually been reported in which, as a result of hypoplasia of the left lung, the heart was displaced to the left side. Reinhold has reported 3 cases: First, a woman aged twenty-four, with a symmetrical thorax and an apex in the left axillary line; there was tympany over the lower portion of the thorax; the autopsy showed bronchiectasis of the left lung and dislocation of the heart to the left. Second, a man of fifty-six years, with similar physical signs. Third, a man of thirty-two years, with an apex beat between the posterior axillary line and the angle of the scapula, and tympany over the lower portion of the left chest. Neisser has reported 4 cases: First, a man of forty-two years of age, with symmetrical, barrel-shaped thorax and an apex beat in the left midaxillary line at the level of the third rib; the diaphragm was high on the left side. Second, a boy of nine years, son of the preceding case, had almost identical physical signs. In 2 additional cases reported briefly there were similar physical signs, with the exception that in 1 there was deformity of the thorax. Heyse reports 1 case, a woman of forty-six years. There was no deformity of the thorax, but evidence of deficiency of the left lower lobe and the heart was dislocated far to the left. Sieveking reports a case with autopsy. The left lung was malformed and also showed evidence of an acquired lesion. The heart was displaced to the left.

These cases seem sufficient to establish the contention that there does exist a condition of hypoplasia of the left lung, with or without a high position of the diaphragm, and with dislocation of the heart to the left. In eventration it has generally been supposed that the dextrocardia is purely mechanical, due to the sliding of the heart down the hill produced by the ascent of the left half of the diaphragm, but such a dislocation could hardly occur as a result merely of hypoplasia of the lung, nor is there sufficient evidence in favor of Doering's view of simple weakness in the left half of the diaphragm. Therefore, it seems to me that we are compelled

to assume that the two conditions coexist; in other words, that in the small number of cases of eventration of the diaphragm hitherto reported, with the possible exception of that of Glaser, there has been not merely a congenital hypoplasia of the lung, but also a hypoplasia or dystrophy of the left half of the diaphragm, and that the dislocation of the heart is due less to the movement upward of the diaphragm *than to the elastic tension of the right lung*. We confess that after reaching this conclusion the pathology of the whole condition is still entirely obscure. We do not know what is the nature of the atrophy of the diaphragm; whether it is due to some lesion of the nervous system, or of the muscle. The cause of the origin of congenital anomalies in the lungs is purely a matter of speculation.

Aside from the pathology of the subject there is but one other point that is of interest, and that is the diagnosis. This is certainly of importance, because in one of the recorded cases, as a result of a mistaken diagnosis of incarcerated diaphragmatic hernia, operation was performed, uselessly of course, but fortunately without disastrous results. The signs in the cases that have been studied clinically have been practically the same. In all there was normal percussion resonance in the upper portion of the left lung; tympany below a certain line, which varied from the second to the fourth ribs; tympany posteriorly, usually from the angle of the scapula down; the ordinary signs of displacement of the heart toward the right; the evidence of the presence of abdominal viscera in the lower portion of the left thorax—that is, gurgling and splashing, especially pronounced when the patient swallowed liquids; often an area of dulness in the lower part when the patient took a considerable amount of food, sometimes associated with distinct Hippocratic succussion. The coin test is negative. Frequently there is an area of dulness posteriorly which appears to be satisfactorily accounted for in 2 cases by the dislocation of the spleen. Litten's phenomenon is usually absent. The movement downward of the area of tympany on deep inspiration was present in 2 cases. The examination with the Roentgen ray in all cases showed that the abdominal viscera were in the lower portion of the left thorax, and this, in 1 certain case, was conclusively proven by introducing a stomach tube filled with mercury, which cast a shadow, and which could be seen coiled up in the position usually occupied by the left lung (Grosser's method). Clinical symptoms may be entirely absent. The gastric disturbances that occur may sometimes possibly be due to other causes; constipation is common enough not to ascribe it to the eventration; but in the case of Widenmann no cause for the hæmatemesis was found, excepting the dislocation of the stomach.

In making the differential diagnosis all those conditions *must*

be excluded that produce tympany in the lower portion of the left chest. Among these probably the most important is pneumothorax. In Strüppler's case puncture was made nineteen times and in ours twice. On no occasion, fortunately, did the needle pierce the stomach wall. In left pneumothorax the respiratory movement is usually absent; the interspaces are dilated; the percussion note is resonant rather than tympanitic; the coin test is positive. In eventration of the diaphragm the respiratory movements are normal; the note in the lower part of the chest is clear and tympanitic, and, in the upper part, is resonant. There is loud gurgling—especially when the patient drinks water—heard over the lower part of the chest. The two conditions have in common dislocation of the heart to the right; Hippocratic succussion, which may disappear, however, in eventration of the diaphragm if the patient has fasted for a long time. If the stomach is inflated in pneumothorax there is distinct bulging in the left hypochondrium. In eventration this is not likely to occur, or is slight, and there is distinct bulging of the lower part of the thorax. Litten's phenomenon is apparently absent in both conditions. One of the most valuable differential signs is the fact that the upper border of tympany moves with respiration in eventration and does not move in pneumothorax. Examination with the Roentgen ray is decisive as regards the differential diagnosis between these two conditions. The presence of a sound filled with some opaque substance in the lower portion of the right thorax indicates that the stomach has risen in that region.

More difficulty would probably be experienced in the case of subdiaphragmatic pyopneumothorax. This is an exceedingly rare condition, and when it does occur is nearly always found upon the right side. The condition is very acute and the patients ordinarily are in a state of collapse, and as the commonest cause is the rupture of a gastric ulcer, a history pointing to the existence of this lesion can ordinarily be obtained. In the small number of published cases (von Leyden, Neusser) the symptoms have been tympany in the lower portion of the thorax, the upper border of which moves with respiration; the physical signs of movable fluid below this area of tympany; dislocation of the liver or of the spleen downward; a positive coin test, and slight, if any, dislocation of the heart. Presumably gurgling over the area of tympany was absent, because it is not mentioned in any of the cases.

The majority of cases of eventration of the diaphragm have been confounded clinically and pathologically with diaphragmatic hernia. According to Strüppler the diagnosis of this condition has been made correctly but nine times during life, not including those cases in which it was made as a result of an exploratory



incision. It is therefore fair to conclude, in view of the fact that more than 500 cases have been recorded, that it is exceedingly difficult. It is interesting to note that 1 of the 9 cases was that of Widenmann, which was subsequently shown to be one of eventration of the diaphragm.

The majority of analyses of the symptoms that have been published are based upon the study of single cases, and therefore are only of suggestive value. Diaphragmatic hernia usually occurs upon the left side, giving rise to an area of tympany in the lower portion of the thorax, causing displacement of the heart to the right and compression of the left lung. There is gurgling over the tympanitic area, and the physical signs, therefore, must be practically identical with those of eventration of the diaphragm, with the possible exception that the upper border of tympany does not move with respiration. Unfortunately in none of the published cases of diaphragmatic hernia, as well as we have been able to ascertain, has attention been paid to this point. In traumatic cases of diaphragmatic hernia the history of severe injury will be of great assistance. Extraordinary variability in the symptoms is common to both conditions, and the case of Glaser shows that signs of incarceration may occur in cases of eventration. Dysphagia paradoxica has not yet been reported in this condition, and is by no means common in diaphragmatic hernia. There was a history of persistent thirst in our case, and this has been noted in several cases of diaphragmatic hernia. Examination with the  $x$ -ray has been shown to be inconclusive, although apparently respiratory movement of the convex line bounding the clear area is in favor of eventration of the diaphragm.

Acquired high position of the diaphragm may apparently occur. Glaser inflated two dilated stomachs ad maximum and found that the diaphragm moved upward a full interspace on the left side. It does not appear that idiopathic dilatation of the stomach produces this displacement. Very little is known of the results of disease of the phrenic nerve. Stockton, however, has reported an extraordinary case which he records as phrenic paralysis, in which there was high position of the diaphragm and tympany in the lower portion of the left thorax. It is not stated whether or not the area of tympany moved up and down during respiration or not, but presumably it did not do so. The symptoms that are described strongly suggest eventration of the diaphragm, but the patient made a complete recovery with disappearance of all the physical signs, indicating that the lesion was transient and not congenital. Without a very clear history it would seem practically impossible to differentiate the two conditions. Cavity or dilated bronchus in the left lung could hardly give rise to difficulty in diagnosis. The character of expectoration,

the absence of displacement of the heart, the amphoric respiration, bronchophony, and pectoriloquy would serve almost immediately to make the diagnosis clear.

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## REVIEWS.

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THE NERVOUS AFFECTIONS OF THE HEART. Being the Morison Lectures delivered before the Royal College of Physicians of Edinburgh in 1902 and 1903. By GEORGE ALEXANDER GIBSON, M.D., D.Sc., F.R.C.P. EDIN., F.R.S.E. Edinburgh and London: Young J. Pentland, 1904.

THE author divides his subject into the two main divisions of sensory and motor disturbances of the heart and devotes to each three lectures. The former division embraces the clinical, pathological, and therapeutic aspects of angina pectoris, and the latter lectures on rate, rhythm, and force. Each lecture is preceded by a brief historical review of the literature and the theories formerly held regarding each subject. A series of diagrams illustrate the text, those which show the distribution of pain to the surface of the body and which indicate the areas of cutaneous hyperæsthesia being especially interesting. A number of sphygmographic tracings illustrate the last three lectures on rate, rhythm, and force, and several of these are particularly instructive, in that they demonstrate the differences which may exist between the radial pulse and the apex beat in a given case.

Professor Gibson departs from the commonly accepted division of angina pectoris into true and false (or pseudo) angina, and argues since angina pectoris is an aggregation of symptoms occurring in various conditions and is not a disease, that it is not logical to make this distinction. He advocates a division into organic and inorganic, and still leaves this point in an unsatisfactory state by saying that "it is not pretended that in the latter class there are no structural changes." It would appear that it would have been better had he chosen two terms which expressed his conception more exactly. Following this classification, he includes neurasthenia, hysteria, reflex agencies, and vasomotor instability among the conditions in which angina pectoris may occur, and adds them with the toxic agencies to the inorganic causes of angina pectoris. His explanation is that in neurasthenia and hysteria the anginous attacks are brought about by debility of the heart and instability of the nervous mechanism. The lectures are the result of such wide reading and experience, and go so fully into the consideration of the physiological and pathological features of cardiac disturbances that the book should be of value to all who are interested in cardiac disease. F. W. S.

THE DISEASES OF SOCIETY. (THE VICE AND CRIME PROBLEM.)  
By G. FRANK LYDSTON, M.D. Philadelphia and London:  
J. B. Lippincott Company, 1904.

DR. LYDSTON has written a very interesting and noteworthy book which deserves careful perusal by all thinking Americans. The study of the criminal classes from a purely scientific standpoint has not made the progress in this country which it has in Europe, and this book may be considered as an attempt at a popular presentation of the results of the investigations of scientific criminologists adapted to the circumstances which prevail in this country. It deals with topics which are of vital importance to every citizen, thus the chapters on Lynching, Anarchy, and the Social Evil which not only go into the causes and the reasons why such things exist, but also give what the author aptly calls their therapeutics, throw light on subjects about which while there is much talk there is really very little knowledge. The sections on what the author terms "anarchy" of government, of law, of politics, and of capital and labor are very slashing and radical, and might be criticised as containing too strong enunciations of the author's personal views.

That part of the work which treats of genius and degeneracy is most interesting. The author accepts the view that "genius is abnormal and both the product and the cause of degeneracy," and then proceeds to adduce facts bearing upon these points. He thinks that while genius may not be hereditary the neuropathic constitution which underlies genius is very distinctly an hereditary trait. Of course, in a work of this nature it is impossible to give complete references, or to always supply facts to support statements, but it is to be regretted that the author yields to the prevalent tendency of writers on such subjects to make isolated statements concerning persons, and to give lists of names of great men accompanied by a sweeping statement that they all were this, that, or the other. As an instance, on page 461 the author states: "Cuvier, Victor Hugo, Chopin, Bruno, Comte, Madame de Staël, Swift, Johnson, Cowper, Southey, Shelley, Byron, Carlyle, Goldsmith, Lamb, Poe, Keats, Coleridge, De Quincey, Chatterton, George Eliot, George Sand, Alfred De Musset, Newton, Chateaubriand, Balzac, Chatham, Burns, Dickens—all these beacon-lights of the history of genius showed indubitable evidences of degeneracy." Such allegations are not only misleading but unworthy of a work which attempts the presentation of scientific facts even if in a popular manner. Dr. Lydston has occupied official positions which have brought him into intimate contact with criminals of all classes and descriptions, and his observations upon these unfortunates are, therefore, entitled to respect. He disapproves most thoroughly of the prison system which prevails in most parts of the United States and of the method of administering justice. He is opposed to

capital punishment, and strongly in favor of the indeterminate sentence. Dr. Lydston is a very thorough-going materialist and also a man of strong convictions who has no hesitation in expressing them. Accordingly, as might be expected, he runs counter to many of the cherished beliefs and opinions of society. The style in which he expresses himself on such topics is at times somewhat florid, and occasionally almost offensive; but we can readily pardon the author when we consider what a really useful book he has produced. It should be read by every thoughtful citizen, and we are sure that even though he may differ from some of the author's conclusions, he will nevertheless find much food for thought in the facts he presents.

F. R. P.

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THE SURGICAL TREATMENT OF BRIGHT'S DISEASE. By GEORGE M. EDEBOHLS, A.M., M.D., LL.D., Professor of the Diseases of Women in the New York Post-graduate Medical School and Hospital; Consulting Surgeon to St. Francis' Hospital, New York; Consulting Gynecologist to St. John's Riverside Hospital, Yonkers, N. Y., and to the Nyack Hospital, Nyack, N. Y., etc. New York: Frank F. Lisiiecki, 1904.

PROBABLY none of the newer surgical fields has excited more general interest in the surgical and medical worlds than the treatment of Bright's disease by operation, and, therefore, this volume is one which is sure to be eagerly read. The most prolific writer on this subject has been Edebohls. The present book is divided into two portions, the first consisting of 142 pages, being the various papers contributed by Edebohls; the latter portion, consisting of 178 pages, is comprised of a minute report of 72 cases which the author had operated upon up to the end of the year 1903, and his conclusions regarding the results. The work covers the whole history of the operative treatment for acute and chronic Bright's disease, and is most interesting and instructive.

Edebohls is naturally more enthusiastic than other surgeons who have had less experience and a higher mortality, but, nevertheless, he shows great fairness, and does not make any rash claims for the operation of decapsulation. He says that the operation is still on trial and must be judged by the ultimate results; that sufficient time has not elapsed since the introduction of the procedure to enable us to give a final judgment. A review of the cases reported must impress the reader with the undoubted position this operation should hold in surgery. It has unquestionably saved lives when nothing else would, and probably it only remains for us to learn how complete and lasting the cure is and to select the proper cases for its employment. Of the 72 cases detailed, but 7 patients died as a

result of the operation. This mortality is strikingly low, when one considers that 16 of the cases reported were patients who were operated upon when death was imminent, due to the late stage of the disease. Seventeen of the cases are reported as cured, 20 as greatly improved, and none any the worse for the operation.

This is a book which we can heartily recommend, not only to every surgeon, but to every internist.

J. H. G.

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A TREATISE ON BRIGHT'S DISEASE AND DIABETES, WITH ESPECIAL REFERENCE TO PATHOLOGY AND THERAPEUTICS. By JAMES TYSON, M.D., Professor of Medicine in the University of Pennsylvania; one of the Physicians to the Pennsylvania Hospital; Fellow of the College of Physicians of Philadelphia; Member of the Association of American Physicians, etc. Second edition. Illustrated. Including a section on the Ocular Changes in Bright's Disease and in Diabetes by GEORGE E. DE SCHWEINITZ, M.D., Professor of Ophthalmology in the University of Pennsylvania; Ophthalmic Surgeon to the Philadelphia Hospital; Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases, etc. Philadelphia: P. Blakiston's Son & Co., 1904.

As stated in the preface, this is a new edition and not a new book, and while much of the matter from the former edition of 1881 has been retained, considerable new material has been added. Entire new sections on the optical changes in Bright's disease and in diabetes mellitus by Professor de Schweinitz, and sections on acute interstitial nephritis and the dietetic treatment of nephritis are to be found. An introductory consideration of the histology and physiology of the kidney has been retained from the former edition, and very wisely, for this makes more clear the statement of the morbid conditions in the discussions of these in relation to the various forms of Bright's disease.

The illustrations and plates are of excellent workmanship, being far superior to most productions of this nature, and the work in the text is equally commendable. To each form of nephritis is devoted a separate section, and the features of each are treated at considerable length.

The section on the diet in nephritis is of especial interest, since there has been some little confusion and difference of opinion in regard to the measures advocated by various authorities. Professor Tyson's views differ from some of the accepted opinions in two particulars mainly. In referring to permitting meat in the diet in nephritis, he states that many are of the opinion that white meat (poultry, game, etc.), is essentially different from the red or dark

meats (beef, mutton, etc.), and that patients are often permitted to eat large quantities of the former, greatly to the detriment of their health. He says that there is not a great deal of difference in the amount of proteids in the various kinds of meats, and that any meat may be injurious, except in small quantities and in cases where the kidneys' function has been fairly well re-established. He also points out the fallacy of using large draughts of water, mineral or plain, in nephritis. It is not generally understood that while the total quantity of urine may be increased by this "flushing" of the kidneys, the percentage of urea is relatively lowered, and the actual amount of urea excreted is not materially increased.

The section on acute interstitial nephritis is devoted to the consideration of a distinct form of Bright's disease, which, while not recently discovered, has been considerably studied in late years, particularly by Councilman. Its pathological distinction, briefly stated, consists in a collection of leukocytes in the connective tissue of the kidney independent of change in the epithelium, and these masses of leukocytes do not tend to become purulent. The condition occurs in the acute infectious diseases, is generally fatal, and its symptoms differ from those of the other varieties of nephritis only in its sudden onset and the very early occurrence of œdema. This form of nephritis is either very briefly alluded to or entirely omitted from articles on nephritis in most of the text-books.

A careful description of the gross and minute pathological changes in the kidney in each form of Bright's disease and the full account of the symptomatology, etiology, complications, and treatment make the book one of especial value in the study of a disease so frequently met and so difficult to treat. Its value is increased when Dr. Tyson's wide experience in the study and treatment of Bright's disease is taken into consideration.

Articles on diabetes mellitus and insipidus are also to be found in the volume, and are included because of the fact that one who makes a specialty of diseases of the kidney sees also many cases of diabetes, and in this way Dr. Tyson has been unusually fortunate in opportunities to study these conditions. These subjects are as skilfully handled and are of as much practical value as are the other subjects treated in the book. The section on diabetes mellitus contains a table, compiled by Dr. Daniel W. Fetterolf, showing the comparative analyses of a number of the products especially prepared for diabetics and much lauded and advertised on account of the small quantities of carbohydrates they are supposed to contain. Other tables showing the increased frequency of diabetes, as indicated by the death rate for this and other diseases, are also of interest. The remarks about diabetic coma, its causation and treatment, are valuable, and the discussion of the relative merits of the different mineral waters used in diabetes should prove useful.

It is to be regretted that the author did not include sections on

tuberculosis of the kidney and nephrolithiasis, and also that in describing the treatment of chronic nephritis he makes no mention of the operation of decapsulation of the kidney as advocated and practised by Edebohls.

F. W. S.

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THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Vol. VIII. MATERIA MEDICA AND THERAPEUTICS, PREVENTIVE MEDICINE, CLIMATOLOGY, SUBJECTIVE THERAPEUTICS, FORENSIC MEDICINE. By GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Post-graduate Medical School. 344 pages. Chicago: The Year Book Publishers, 1904.

THIS volume, edited by Satler, Favill, Bridge, Brower, and Moyer, presents a rather brief but discriminating review of the progress in these departments during the past year. Its merit lies in the convenience of size and division of subjects, and it should be useful for the general practitioner, while the specialist will find the important advances chronicled. We note marked improvement over its predecessors.

R. W. W.

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OUTLINES OF PHYSIOLOGICAL CHEMISTRY. By S. P. BEEBE, PH.D., Physiological Chemist to the Huntington Fund for Cancer Research, and B. H. BUXTON, M.D., Professor of Experimental Pathology, Cornell Medical College. New York: The MacMillan Company. London: MacMillan & Co., Ltd., 1904.

THIS book of 195 pages sets forth the principal chemical compounds found in the human body, and shows their relationship to other organic substances. Some knowledge of inorganic chemistry is presupposed, but in order to carry the reader on from fundamental facts, the first chapter deals with the theory of solutions and ionization. The subject of organic chemistry is then briefly reviewed, covering the first hundred pages of the book. Here the relations of the organic substances to physiological processes is seldom mentioned, and this part of the work differs very little from what one expects to find in a brief work on organic chemistry.

The last three chapters are on the proteids, enzymes, and disease and immunity. Here chemical processes of physiology are brought out briefly. The work gives the impression of being somewhat overcondensed. The style, however, is clear, concise, and to the point. Many diagrams help to make clear the chemical formulæ in which the book abounds.

As a text-book it will no doubt be of use, since it briefly covers ground important in medical education.

W. T. L.



HEALTH, STRENGTH, AND POWER. By DUDLEY ALLEN SARGENT, A.M., Sc.D., M.D., Director of Hemenway Gymnasium, Harvard University. Illustrated. New York and Boston: H. M. Caldwell Co.

THE author gives an impressive argument in favor of regular systematic exercise by people of the industrial class, who disregard or are in ignorance of the vital importance of the development of all the muscles. He cites the deterioration of the physique of the British recruits at the time of the South African War, and very reasonably states that this physical decadence should alarm all civilized nations. To check this, which is directly traceable to modern conditions in the cities, he advocates the establishment of gymnasia which will attract those persons who are put to work at an early age and who, from the increasing specialization of their work, are accustomed to use but a few groups of muscles. It is evident that many orthopedic conditions could be prevented or cured if exercises were undertaken which would give a symmetrical development and correct faulty postures.

Full advice is given in regard to bathing, clothing, diet, and rest; and since on all these points erroneous opinions are commonly held, the instructions given should be of great value. Separate chapters are devoted to the discussion of exercise for children, women, the middle-aged, and the old, and also to methods for the treatment of obesity and leanness.

Fifty-six forms of exercise are described, and Dr. Sargent has adopted the plan of giving each a character and name which connects it with some occupation or sport, as wood-chopping, throwing a ball, etc. While this adds the elements of a game, and is undoubtedly desirable for children, it seems to make the exercises more cumbersome and complicated than is required for the muscular movements aimed at, and thus makes them less suitable for adults.

An excellent feature of the system is the recognition of the necessity for relaxation of the muscles and proper attention to respiration, which is in marked contrast to some of the recently advocated systems.

F. W. S.

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REGIONAL MINOR SURGERY: Describing the Treatment of those Conditions Daily Encountered by the General Practitioner. By GEORGE GRAY VAN SCHAIK, M.D., Consulting Surgeon to the French Hospital, New York. Second edition. New York: International Journal of Surgery Co.

WE are glad to see the second edition of this little book, which fills its purpose in a very satisfactory manner. In a review of the previous edition, we had an opportunity to mention its good points, so

that the repetition of them is unnecessary. We can, however, repeat that the general practitioner doing occasional surgery, and even the experienced surgeon, will find in it many valuable suggestions in the treatment of minor surgical conditions. J. H. G.

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MEDICAL LABORATORY METHODS AND TESTS. By HERBERT FRENCH, M.A., M.D. (Oxon.), M.R.C.P. (Lond.), Medical Registrar, Guy's Hospital; Gillson Scholar, Society of Apothecaries of London; Radcliffe Travelling Fellow, Oxford University. Chicago: W. T. Keener & Co., 1904.

THIS small book of 150 pages contains briefly the principal simple laboratory tests that are made upon urine, blood, sputum, pus, gastric contents, and feces, together with short accounts of the microscopic examination in skin diseases, examinations of serous exudates, cerebrospinal and cystic fluids, and tests for the commoner poisons. In order to include so much in so small a book, a tabulated method is employed. The various methods are briefly but clearly given in a well-arranged manner. The relative importance and sources of error in these methods are mentioned, but explanations of the tests are largely omitted. The book should serve as a handy reminder to the laboratory worker of how the various common laboratory tests are made.

The book contains a number of illustrations taken apparently from free-hand drawings, and which often convey very little meaning. Otherwise, the book is all it claims to be. The statements contained in it are, for the most part, correct, but the few errors that we have found are largely faults of omission rather than commission.

G. C. R.

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A PRACTICAL TREATISE ON GENITOURINARY AND VENEREAL DISEASES AND SYPHILIS. By R. W. TAYLOR, A.M., M.D. Third edition, thoroughly revised. New York and Philadelphia: Lea Brothers & Co.

ANY work on venereal diseases from the pen of Dr. Taylor deserves and is bound to receive prompt and eager attention by reason of the long and extensive experience of the author. The present treatise fully justifies one's expectations and ably realizes the wish of the writer to present "a practical, up-to-date, compact treatise." The chapters on Gonorrhœa are thoroughly in accord with the trend of modern thought, and the subject is discussed in a most comprehensive manner, nitrate of silver being considered as the ideal agent for the treatment of the affection. We cannot, how-

ever, agree with the writer's caustic criticism of what he is pleased to term "so-called ideal substitutes for nitrate of silver," some of which are mentioned as "therapeutic curiosities," and all of them as "hybrid" preparations.

As might be expected from the author's great reputation as a syphilographer, the portion of the work devoted to the discussion of syphilis deserves the highest praise. Indeed, it would be hard to find anywhere a more comprehensive treatise on syphilis than the writer has given us here. In the section devoted to genitourinary affections the author's desire to present the subject in a compact form has resulted in some places in a want of completeness in the discussion. As an example of this, may be mentioned the consideration of the operative treatment of hypertrophy of the prostate, to which only three pages of the work are devoted.

The volume as a whole stands in the front rank of treatises on this subject, and should be in the possession of every practitioner of medicine.

H. M. C.

**DIET IN HEALTH AND DISEASE.** By JULIUS FRIEDENWALD, M.D., Clinical Professor of Diseases of the Stomach in the College of Physicians and Surgeons, Baltimore, and JOHN RUHRAH, M.D., Clinical Professor of Diseases of Children in the College of Physicians and Surgeons, Baltimore. Philadelphia, New York, and London: W. B. Saunders & Co., 1905.

THIS volume on dietetics opens with a consideration of the principles of digestion, its chemistry and physiology. The transformation of the different forms of proteids, fats, and carbohydrates in the various parts of the alimentary tract is briefly described. Diet for healthy individuals is then discussed, and such factors as age, climate, and idiosyncrasy are mentioned as influencing the selection of our foods. Foodstuffs are themselves classified in the succeeding chapter and several pages are devoted to the alcoholic beverages. Analyses of most of these are given, with accompanying tables, showing their relative percentages of alcohol and their various chemical constituents.

The sections on milk modification and infant-feeding are noteworthy. In the former, not only is there a good introductory explanation of the general principles of the modification of cows' milk, but also the best-known methods are explained, and a series of formulæ are worked out, the results being tabulated for instant reference.

The latter half of the book takes up the subject of diet in disease. The dietary treatment of the fevers, the infectious diseases, acute and chronic digestive ailments, gout, diabetes, and so on, is repre-

sented systematically. Full information is given as to the hours for feeding, preparation, and administration of the various foods, with lists of a number of useful receipts.

At the end of the volume are figures showing the different cuts of beef, mutton, and pork, and a long list of the chemical composition of American food materials. The book is practical, and the recipes and diet-lists should prove exceedingly useful. A. N.

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THE MEDICAL EPITOME SERIES. TOXICOLOGY. A MANUAL FOR STUDENTS AND PRACTITIONERS. By EDWIN WILLES DWIGHT, M.D., Instructor in Legal Medicine, Harvard University. Series edited by VICTOR COX PEDERSEN, A.M., M.D., Instructor in Surgery and Anæsthetist and Instructor in Anæsthesia at the New York Polyclinic Medical School and Hospital, etc. Philadelphia and New York: Lea Brothers & Co.

THIS book of 295 pages consists of a well-arranged brief treatise on toxicology. The various common poisons are systematically treated. Each substance is dealt with somewhat as follows: the method for obtaining it from nature, its properties, commercial and medical use; its criminal use, tonic dose, and action are briefly discussed. Then follows a few paragraphs on the symptoms produced by the poison and their treatment, the post-mortem appearances caused by the various substances, and a few simple tests for their recognition. Actual cases from the literature are used to illustrate the effects of the various poisons—an especially good feature—as it adds much to the interest of the book, and impresses the practical bearing of the subject.

The size of the book should make it suitable for a text-book, and at the end of each chapter several questions are added which might be used for quizzing. The author's style is simple, direct, and clear. The printing of the text is noticeably good. G. C. R.

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MEDICAL DIAGNOSIS. SPECIAL DIAGNOSIS OF INTERNAL MEDICINE. A HANDBOOK FOR PHYSICIANS AND STUDENTS. By Dr. WILHELM V. LEUBE, Professor of Medicine and Physician-in-chief to the Julius Hospital at Würzburg. Authorized translation from the sixth German edition. Edited with alterations by JULIUS L. SALINGER, M.D., late Assistant Professor of Clinical Medicine in the Jefferson Medical College; Physician to the Philadelphia Hospital. New York and London: D. Appleton & Co., 1904.

LEUBE's *Diagnosis* is so well and favorably known through its six German editions that it seems a work of supererogation to go

at length into descriptions. The work, which for the first time has been translated into English by Dr. Salinger, will prove of interest and value to physicians. Certain small additions have been inserted by the translator where, for one or another reason, they seemed necessary; thus, in all respects, bringing the subjects up to the level of the times. Leube's *Diagnosis* is among the foremost, if not the foremost, work on the subject, and this able translation brings it within the range of the non-German-reading students and physicians.

J. N. H.

THE PATHOLOGY OF THE EYE. By J. HERBERT PARSONS, B.S., D.Sc. (Lond.), F.R.C.S. (Eng.), Assistant Ophthalmic Surgeon, University College Hospital; Curator and Pathologist, Royal London (Moorfields) Ophthalmic Hospital; Lecturer on Physiological Optics, University College, London. Volume I., Histology. Part I. New York: G. P. Putnam's Sons. London: Hodder & Stoughton, 1904.

THIS is the first complete treatise upon the pathology of the eye that has yet appeared in any language. It is pleasant to have such a book, the first of its kind, in English. Better still, the dress is not only English, but the author has not resorted to mere transcriptions from German monographs; it bears the stamp of original research, besides such a comprehensive grasp of the subject as to justify the author in his undertaking. The work will consist of four volumes. The first volume deals with the pathological histology of the anterior portion of the eyeball as far as the lens, including the bacteriology of the conjunctiva. The normal histology of the parts considered is briefly described. This volume is profusely illustrated from photographs of specimens.

This work is not intended for elementary instruction. General knowledge of histology, both normal and pathological, is required on the part of the reader who would benefit from it; nor should such knowledge have been acquired merely from reading; practical work at first hand in a laboratory is essential for the student who would derive the advantages which this treatise is capable of affording.

At the conclusion of each section a reference-list of papers is appended.

The mechanical execution of the book leaves nothing to be desired.

As the author observes, most of the problems which are here dealt with remain to be solved; the work brings together the data so far as known, and the difficulties to be overcome, and will, no doubt, long remain a standard of reference for all those who concern themselves with the scientific basis of ocular pathology.

T. B. S.

A PHILOSOPHY OF THERAPEUTICS. The foundation of which rests on the two postulates: First, that it is the human organism that is the active factor in the healing of the sick, and not drugs, and, second, that there are two therapeutic laws. By ELDRIDGE C. PRICE, M.D. Baltimore: Nunn & Co.

THE author of this volume desires to present to the reader the evil of ultra-conservatism on the part of the advocates of the different schools of medicine. There is considerable space devoted to the consideration of the laws enunciated by Galen and Hahnemann. The fact that there is much good to be found in the ideas of both schools is emphasized. It is a plea for less prejudice and more knowledge. He contends that only by this means can the physician attain the ideal of medical science, "the greatest good to the patient." Unfortunately, the author himself, in many parts of his work, assumes the character of a special pleader for his own views. He is of the opinion that we are too prone to accept statistical results without first viewing the conditions which influence the facts on which the statistics are based. The object of the Baltimore Medical Investigation Club is mentioned in this connection, and the investigation of several drugs by it cited as examples of the proper method of procedure. The style is rather wordy, and there are some typographical errors.

A. N.

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NOTHNAGEL'S ENCYCLOPEDIA OF PRACTICAL MEDICINE. TUBERCULOSIS AND ACUTE GENERAL MILIARY TUBERCULOSIS. By Prof. Dr. G. CORNET, of Berlin. Edited, with additions, by WALTER B. JAMES, M.D., Professor of the Practice of Medicine in the College of Physicians and Surgeons (Columbia University), New York. Authorized translation from the German, under the editorial supervision of ALFRED STENGEL, M.D., Professor of Clinical Medicine in the University of Pennsylvania. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THIS is the seventh volume of the Nothnagel series and is devoted to the study of tuberculosis, including practically all that is known of the subject from every point of view.

The work is divided into two parts—I. Tuberculosis, and II. Acute General Miliary Tuberculosis—and these two parts are in turn subdivided into many interesting chapters. In selecting for particular mention any chapter to the exclusion of others in this excellent book one is, in truth, making unfair distinctions, but we may perhaps be forgiven in so doing, on the ground that these particular chapters are of great popular medical and lay interest. Such chapters as those on the Tubercle Bacillus, with reference to morphology,

biology, chemistry, etc.; the modes of Invasion, Infection, Predisposition, and Prophylaxis are full of the very latest scientific thought presented in the clearest terms.

Professor Cornet takes a very strong position in regard to the frequency of infection as the agent in the spread of this widely fatal disease. In the course of his argument, in a most original manner, he points out many fallacies in statistics which might lend an undue weight to either the theory of predisposition or that of heredity, but which, when properly interpreted, serve but to strengthen the view that infection plays the leading role, independent of any hereditary or other predisposing cause.

The author's explanation of the frequency of tuberculous lung affections in the wake of certain diseases (whooping-cough, measles, influenza) is plausible and interesting. He ascribes such immunity from phthisis as does exist to the action of the cilia of the epithelial cells lining the air-passages in mechanically brushing back partially inhaled bacteria. In those diseases most commonly followed by phthisis there is a very notable involvement of these same epithelial cells, with the possible result of so crippling the cilia that this repellant function is abrogated. He points out the difficulty of claiming for any organ a greater or less degree of susceptibility, judging merely from the frequency with which this particular organ is attacked, unless the observer is in possession of the knowledge of the mode of invasion. Bovine and human tuberculosis are believed to be caused by the same bacillus, though modified in many respects by its sojourn in the animal or human host.

In discussing prophylaxis, the value of public education in regard to the method of the spread of tuberculosis is pointed out. The individual afflicted with the disease has it within his power to render himself innocuous to his family and the community at large by attention to the one detail which decency and unselfishness should dictate, and that is never to spit on the floor or street, but always, when it becomes necessary, to spit into vessels containing a little fluid. No less interesting are the remaining chapters on Symptoms, Course, Diagnosis, Prognosis, and Therapy. Space, however, will not permit of any but this passing mention.

Never before has this great subject been treated so exhaustively, so clearly, and so intelligently, and Professor Cornet and the editors are to be most heartily congratulated on their work.

J. N. H.

# PROGRESS OF MEDICAL SCIENCE.

## MEDICINE.

UNDER THE CHARGE OF

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**A Case of Suppurative Myositis Caused by Micrococcus Gonorrhœa (Neisser).**—HARRIS and HASKELL (*Johns Hopkins Hospital Bulletin*, December, 1904, p. 395) comment on the multiplicity of the complications of gonorrhœa. They have searched the literature for cases of myositis following this disease, and give abstracts of 7 cases in which a myositis due to the gonococcus was believed to exist. In 6 of these a suppurative myositis was believed to exist, but the bacteriological proof was not sufficiently convincing in any single instance to definitely warrant the opinion that the gonococcus was the cause of the inflammation. Their own case concerned a woman, aged thirty-four years, who since the birth of her last child, eleven months before, had suffered from leucorrhœa. She had had it on previous occasions, and this symptom constituted the only evidence of a gonorrhœal infection. Four weeks before she was admitted to Dr. Osler's wards in the Johns Hopkins Hospital a lump the size of a hen's egg developed in the right calf muscles, giving place later to a diffuse boggy swelling. Several months before she came under observation another swelling, also about the size of a hen's egg, appeared over the lumbosacral region. The abscess in the calf muscles was aspirated and a small amount of pus obtained for bacteriological examination. The pus showed a diplococcus which in its staining and cultural characteristics conformed in every way with those of the gonococcus. The abscess was eventually incised and it was found to contain about one and a half pints of pus. It was situated beneath the gastrocnemius and soleus muscles and extended up into the popliteal space. There had been considerable sloughing of these muscles and their tendons. The abscess in the lumbosacral region was incised and was found to contain about three ounces of pus. It extended up into the erector spinæ muscles on either side, which, with their tendons, showed considerable sloughing. The bacteriological examination of the pus obtained from the abscesses at



operation demonstrated conclusively the presence of the gonococcus. A feature of interest in this case was that there was no co-existent arthritis nor was there any history of its having previously been present.

**Abnormalities in the Feces in Disease of the Pancreas.**—URY and ALEXANDER (*Deutsche med. Wochenschrift*, 1904, xxx. p. 1311), on the basis of a number of cases and a general survey of the literature, point to the importance of careful examination of the feces in suspected disease of the pancreas, while emphasizing the reserve which must be exercised in interpreting the results. The two points of special interest are the determination of the fat and proteid digestion. There are three possibilities in reference to abnormal fat content of the feces in pancreatic disease. There may be an increased amount of fat with diminished fat splitting, an increased amount of fat with normal splitting, or a normal amount of fat with diminished splitting. It is of great importance in these estimations to regulate accurately the amount and character of the ingested food. Fat kept within the bounds of assimilation is normally well utilized (7 per cent. to 10 per cent. loss), and the limit is high, reaching, with individual variations, about 350 grams for butter. The tolerance for fats is much diminished in disease of the pancreas, and the limit of assimilation relatively low, so that by carefully regulating and changing the diet defects in pancreatic secretion might be recognized at an early stage. Conclusions from the amount of fat in the stools can, however, only be drawn under the following conditions: There should be no jaundice, as absence of bile may of itself cause steatorrhœa; the fat should not be administered emulsified, and there should be no diarrhœa. If diarrhœa be present, it may be checked with opium. Even under these precautions the results are of value in diagnosis only when considered in relation to other symptoms. Marked steatorrhœa may occur in disease of the small intestine, with diminution of its absorptive power, and in diseases interfering with the flow of fat through the lacteals, as enlarged mesenteric glands and tuberculous peritonitis. On the other hand, one meets with cases of almost complete destruction or atrophy of the pancreas, in which, during life, fat digestion is perfect. What Ury and Alexander consider almost pathognomonic of pancreatic disease is the discharge of large quantities of liquid fat after the solid, formed feces have been passed. Most cases of steatorrhœa are associated with an excessive number of well-preserved muscle fibres in the stool, although either condition may occur without the other. This is not surprising, in view of the results which have established the independence of fat and proteid digestion. Muscle fibres, of course, occur in normal stools, and to recognize an azotorrhœa, not more than one-half pound of tender meat a day should be allowed. The significance of this condition is likewise relative and occurs in various affections disturbing the movements, secretion, and absorption of the small intestines. A third point of some importance is the evacuation of relatively large quantities of solid feces. Nobel thought the absence of the products of putrefaction was an important diagnostic aid, but Ury and Alexander found a normal amount of aromatic oxyacids in their cases. In diabetes, as a rule, both fat and proteid digestion are well preserved. In certain cases, however, with marked steatorrhœa and azotorrhœa, extensive involvement of the pancreas has been correctly diagnosticated. Naunyn, however, cautions against too great reliance on these symptoms.

**Hereditary Syphilis in the Second Generation.**—BOECK (*Berliner klin. Wochenschrift*, 1904, xli. p. 968) cites four instances in which the evidence appears to him conclusive that the mother, herself the subject of inherited syphilis, transmitted the taint to her offspring. In the first case the grandmother, at the age of eighteen years, had been treated for secondary lues in 1854; the mother, at the age of two months, for hereditary syphilis in 1860; while the child, aged four to five months, was brought to him with definite lesions of inherited disease in 1889. The mother at this time had Hutchinsonian teeth and typical scars about the mouth, but no sign of secondary lesions. No history could be obtained to support the suspicion of a reinfection. She had had no miscarriages or premature births, but in 1883 was delivered at the lying-in hospital of a healthy child, which she had by another man. Examination at that time revealed no evidence of syphilis either in mother or child. By her husband, the father of the syphilitic infant, she had had, three years before, a perfectly healthy child, and on most careful examination nothing could be found in the father to justify any suspicion of disease. In the second instance the grandmother, when nineteen years of age, was treated at the clinic for a chancre of the lip and subsequently for secondary symptoms. Three years later she gave birth to a dead child. After this, however, she had three children, all of whom lived. The eldest of these presented herself, at the age of twenty years, with her first child, which was evidently the subject of inherited syphilis. The mother had no knowledge of the disease in herself, but presented characteristic scars about the mouth. There was no evidence that she had suffered from the acquired form of the disease. In the third instance, a woman aged twenty-one years, with Hutchinsonian teeth and scars of old rhagades, brought to the clinic her child of five months, who was affected with inherited syphilis. Six months previously the grandmother had sought advice for a tertiary tuberculo-serpiginous syphilide on the left forearm. The same mother bore a second child five years later, which was also the subject of inherited syphilis. In her case there was likewise no reason for suspecting a reinfection. The father of these two children and the father of the child in the second case could not be examined, but Boeck lays little emphasis upon this, as he considers infection from the father excessively rare, if at all possible. In an experience of thirty years he has met with not a single instance in which the facts have obliged him to admit paternal infection of the offspring, and this view is supported by many other observers. That the mother of the first child had previously borne two healthy infants is nothing anomalous, as the more remote the date of infection of the mother, the more uncertain and variable will be the fate of the offspring. The time between the infection of the mother and the birth of the children is not too long to admit of her giving them the disease, as in the acquired form women may bear syphilitic children twenty years or even thirty-seven years after inoculation.

In this relation it is interesting to note the opinions of JONATHAN HUTCHINSON, which appear on page 977 of the same journal:

"1. I have never had an opportunity for personally investigating a case in which the evidence convinced me that syphilis had been transmitted by inheritance to the third generation. Several very interesting ones have been brought under my notice in which at first the facts seemed conclusive, but in which on further examination they broke

down. For the present I do not believe in the possibility of such transmission.

"2. No doubt can, I think, be reasonably entertained as to the transmission of syphilis by the male parent without direct infection of the mother. This is in England by far the most common form of transmission, for it is very rare that married women have suffered from primary disease. . . ."

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## SURGERY.

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UNDER THE CHARGE OF

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**Duodenal Ulcer and its Treatment.**—D'ARCY POWER (*British Medical Journal*, December 17, 1904) states that the subject of duodenal ulcer has not yet received adequate attention, though its onset is severe and the sequelæ may be dangerous. It is usually thought to be of rare occurrence, but during the last few years the author has had the opportunity of operating upon 7 cases and observing some others. These cases grouped themselves sharply into two classes: those in which the ulcer had perforated and those in which there was no perforation. The cases which perforated required immediate surgical treatment and were sutured with more or less success. Those which did not perforate were either treated at once on account of hemorrhage or came for treatment many years afterward in consequence of duodenal narrowing due to cicatrization of the ulcer. The non-perforating cases were treated by retrocolic gastrojejunostomy. As all the cases were in males it may be presumed that this condition is more common in this sex than in females. After noting in detail the symptomatology of the two classes of cases the author fully considers the question of diagnosis and states that it should be easy to diagnosticate the cases where perforation has occurred, but in practice it is often found to be a matter of very great difficulty. The symptoms are not characteristic and so the diagnosis is often left in abeyance, in the hope that a few hours' delay will render the signs and symptoms more definite. Such advice is likely to prove fatal, for, instead of making the diagnosis clearer time only renders it more obscure. The slight clues which could be picked up shortly after the onset, are soon masked by the peritonitis which follows. Delay not only allows the peritonitis time to develop, but it permits the extravasated contents of the alimentary canal to gain access to the innermost recesses of the peritoneum, so that a subphrenic, pelvic, or iliac abscess may still further complicate a condition which is well-nigh desperate. A rapidly increasing pulse rate

with acute abdominal pain and but slight objective symptoms is an indication for an exploratory operation. The diagnosis becomes even more obscure without operation, and the case may be mistaken for pneumonia, appendicitis, or peritonitis, due to causes other than intestinal perforation. The lesson to be learned from the cases that have perforated is to operate early. The perforation often takes place without warning, and it thus occurs in persons who are otherwise in excellent health. Such persons bear an abdominal operation very well, and it is better to open an abdomen needlessly than wait until the symptoms of peritonitis make an operation imperative. The diagnosis of the non-perforative cases is even more difficult, for the reason that there is no pathognomonic sign of non-perforating ulcer of the duodenum. After noting in detail the various symptoms the author reaches the following conclusions: (1) Duodenal ulcers are not very uncommon. (2) So far as he has seen them, duodenal ulcers are single and are more common in men than in women. (3) Duodenal ulcers may perforate and cause acute symptoms, or they may heal, and by cicatrization lead to symptoms of chronic duodenal obstruction. (4) The sequelæ of a healed ulcer may be so remote that the symptoms are mistaken for those due to cancer of the pylorus, and the patient is allowed to drift from bad to worse under the erroneous notion that he is bound to die. (5) There is no means of recognizing the existence of a duodenal ulcer in a great many cases until it perforates or the results of its cicatrization become manifest. (6) The treatment of duodenal ulcer consists (a) in the direct suture of a perforated ulcer, the prognosis being less favorable than in similar cases of perforation; (b) the performance of gastrojejunostomy in cases of dilated stomach due to duodenal constriction, the prognosis being the most favorable of all the conditions for which this operation is performed at the present time.

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**The Intravenous Injection of Antitoxin in Diphtheria.**—BIERNACKI and MUIR (*Lancet*, December 24, 1904) state that they are familiar with the work of Cairns, who has claimed increased efficacy for this method and who has stated that there resulted a quick subsidence of the glandular enlargement, a strikingly rapid decline in the toxæmia, and in pneumonic cases a marked diminution in the restlessness. In 50 cases, 20 of which were treated by this method, there were only 3 deaths, a mortality of only 6 per cent. Of these 17 were tracheotomy cases, with only 1 death, a mortality of only 5.8 per cent. The authors state that they tried the method in 7 cases with 5 deaths in one series, and in another, in 38 cases with 3 deaths.

After reporting these cases in detail they state in conclusion that in attempting to estimate the beneficial effects of antitoxin given intravenously those cases must be discounted in which a marked improvement follows intubation or tracheotomy, since this may be due mainly or entirely to relief of the obstruction. Nevertheless, it will be noted that of 9 cases operated on early, only 1 died, and this must be regarded as a low mortality. Even in cases other than laryngeal, it would seem very difficult if not impossible to say of any individual patient that a better result was obtained than might have followed subcutaneous injection. However, there was a fatality of 3 in 38 selected severe cases. This result seems to be in favor of the intravenous method. At the same time, although many of the cases treated were undoubtedly

very severe, there has been a general fall in the fatality of diphtheria in the district, and this leaves room for speculation as to whether the subcutaneous method might not have yielded better results than in the past.

**The Germ Cell Theory of Cancer.**—GRUNBAUM (abstract in the *British Medical Journal*, December 17, 1904). The explanation of the genesis of malignant growths has been brought nearer to us by two notable investigations. They are (1) the proof of the morphological continuity of the germ cells, and (2) the discovery of heterotype mitosis in malignant tumors. They corroborate and fortify each other in a remarkable way. Until recently it was always taught that the sexual cells arose in the embryo from a layer of peritoneal epithelium, known, it is true, as the germinal layer, but not otherwise distinguished in origin from the remaining cells of the embryo. It is to the credit of Dr. James Beard to have definitely disproved this method of formation and to have clearly shown the morphological continuity of the germ cells. He has combined with this the suggestive hypothesis of an antithetic alteration of generations also in man.

Put very briefly, this may be stated as follows: After the union of the sperm and the egg, there is formed by the subdivision of the united cell what corresponds to a larva or trophoblast; in man the chorion. From one of its cells there is formed, as it were, a number of spores. One of these spores ultimately becomes the embryo, which includes within itself the remaining spores to become its sexual cells, which are thus not formed from the embryo, but are handed down to it, and for which it merely forms a home.

In passing to their proper position in the embryo these germ cells may go astray, and may in some animals be demonstrated for a time in all sorts of abnormal positions. Dr. Beard was also the first to suggest that the aberrant germ cell might be the origin of cancerous growths, although he now prefers to consider it as an identical twin, namely, an embryo developed, or rather undeveloped, from the same germ cell. The former idea would seem to be the preferable one.

But what proof is there of any connection between a germ cell and a malignant growth? This has been supplied by the discovery of Professor J. B. Farmer with Messrs. Moore and Walker. They found in malignant tumors a form of nuclear division which normally occurs only in the sexual cells, among the spermatozoa and ova. One of the distinguishing features of this heterotype mitosis is the formation by the dividing cells of only half the normal number of chromosomes. Both this and the other characteristics were observed in the cells of malignant growths; there must, therefore, be something in common between the germ cell and the tumor cell.

In innocent tumors they were unable to find this form of nuclear division and considered its absence an essential difference between the two forms of growth. It would seem to corroborate the view that the distinction between malignant and innocent tumors is not fundamental. We know that clinically one form may pass into the other.

The heterotype mitosis does not supervene at once in the evolution of the sexual cells. In the testis it is not before the third division, and in the ovary when the membrana granulosa begins to proliferate, and the discus proligerus is formed; definite proof of their non-somatic

origin. In the same way heterotype mitosis may not occur at first in tumors, and during this stage they are not malignant, but when it supervenes they become so. Why this change should occur is another matter; but it is no more mysterious in the case of a tumor than in that of the testis or ovary.

Given the cell or cells of the potential growth it seems not improbable that the toxin of a parasite, the short stimulus of a trauma, the long-continued stimulus of chronic irritation or the chemical conditions of disordered metabolism, might suffice to let loose their energies and thus one or all of the alleged causes in turn have their share.

The sign-post of further investigation of the problem points along the road of embryological and cytological inquiry.

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## THERAPEUTICS.

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UNDER THE CHARGE OF

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ASSISTED BY

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**Hepatic Opoththerapy.**—DR. JULES REYNAULT reports an instance of cirrhosis of the liver, with splenomegaly, ascites, and œdema of feet which had resisted other modes of treatment, but in which the following mode of procedure achieved a rather remarkable result. The patient was given the following prescription: ox gall simmered over a slow fire until it had reached a syrupy consistency, 5 drachms; powdered rhubarb and powdered cinchona, equal parts, q.s.; make 40 pills. Four of these were taken daily and the following diet was ordered. Each day, calf, pork, or sheep liver, raw or slightly broiled, 4½ ounces; raw spleen of pork or sheep reduced to a pulp, 1½ ounces; milk 2 to 3 quarts. After seven days the patient was much improved and all the symptoms were less marked. The spleen pulp was now stopped because of the nausea which it had produced, the liver was reduced to 3 ounces and the pills to two per day. Eggs were allowed. After three weeks of treatment the special diet was abandoned and a few days later the pills, and the patient returned to work. The amelioration is permanent, the liver and spleen, while not so small as normal have diminished in size and the general condition is excellent.—*Revue de therapeutique*, 1904, No. 20, p. 695.

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**The Action of Radium in Cutaneous Affections.**—DR. SCHOLTZ states that the action of the rays emanating from radium resemble the x-rays, but differ in the following points: (1) Radium acts more energetically upon the vessels, its deep action is more marked, and it possesses

bactericidal properties. (2) Radium exercises a more intense and more favorable effect than the  $x$ -rays upon malignant cutaneous neoplasms (especially carcinomata) and upon small telangiectases and angiomas. (3) Radium may easily be employed within the cavities of the organism.—*Revue thérapeutique*, 1904, No. 20, p. 709.

#### Therapeutic Indications Furnished by Sphygmometer in Enteric Fever.

—DRS. CARRIERE and DANCOURT consider that it is necessary to distinguish the cases with hypotension from those with hypertension. Hypertension is likely to precede the onset of complications, congestive or hemorrhagic, depending upon the localization of the hyperæmia. To avoid these complications we should combat the excess of arterial tension. This may be done by means of the vasodilators and in cases of heart weakness by these in connection with heart stimulants. One may use amyl nitrite, the other nitrites or trinitrin, but the author gives preference to spiritus ætheris nitrosi, of which he gives 20 to 100 drops during the twenty-four hours. In elevating arterial tension we may use agents which act upon the peripheral vessels by vasoconstriction or those which stimulate the heart's action. In enteric fever the vasoconstrictors are dangerous because of the increased work which they impose upon a previously weakened heart. The authors reject the vasoconstrictors, choosing instead cardiac stimulants, of which digitalis, caffeine, and sparteine are the most effective. They usually prescribe the first in the form of the infusion. If intolerance occurs, caffeine is substituted.—*Revue de médecine*, 1904, Nos. 7 and 8, pp. 537 and 643.

#### Urotropin, Methylene Citric Acid and Urotropin Methylene Citrate.—

DR. ARTHUR NICOLAÏER records his exhaustive studies of these drugs, confirming his statement made in 1895 that urotropin in  $7\frac{1}{2}$  grain doses 2 or 3 times a day in  $\frac{1}{2}$  pint of water is harmless and soon after administration appears in the urine, that the urine, without losing its acidity acquires uric acid solvent properties and an inhibitory action on bacterial growth except upon that of the tubercle bacillus. At times there occurs non-tuberculous bacterial infection in which the desired effect of urotropin is not obtained; consequently experiments were made with helmitol (urotropin methylene-citrate or new-urotropin). First, experiments were made with methylene citric acid from which it was concluded that this drug did not give off formaldehyde in the urine as does urotropin and may produce skin eruptions, and digestive disturbances. These same objections hold good in regard to citarin, the sodium salt of methylene citric acid. With regard to helmitol it was proven that in doses which are the coefficient of the usual urotropin doses—i.e., which are two and one-half times as great as the latter, helmitol is effective in exactly the same conditions in which urotropin is effective and ineffective in exactly the same cases in which urotropin is ineffective. It has also been shown both bacteriologically and clinically to be dependent for its therapeutic efficiency upon its urotropin content and by reason of the contained methylene citric acid to be capable of causing unpleasant by-effects.—*Deutsche Archiv für klinische Medizin*, 1904, Nos. 1 and 2, p. 181.

**Thiol in Dermatology.**—M. LEREDDE considers that this substance, which is derived from oil of wood-tar and occurs in either powdered

or liquid form, is useful in dermatological practice, where it may be employed in solutions, ointments, glyceroles, etc., of from 5 to 10 per cent. strength. Its chief indications are in eczema and other pruriginous affections. In the acute type of the former condition thiol is useful in the declining stages. In chronic eczema it is also useful in combination with other substances. Its antipruritic action is excellent, and it may be employed in acute pruritus, prurigo, licheniform lesions, etc. Thiol combined with other antiparasitics is useful in the seborrhœides, intertrigo, psoriasis, artificial dermatites, and it acts well in the acute dermatoses of infants. No bad effects are attendant upon its use, and it is worthy, according to the author, of more general employment.—*La presse médicale*, 1904, No. 91, p. 727.

**Thigenol in Gynecology.**—DR. RAOUL BLONDEL has employed this agent for a year, both in dispensary and in private practice, and considers it a very valuable one. Its action is that of ichthyol, but it is to be preferred to this substance, since it is more effective and has none of the disadvantages of the latter, either in regard to odor or to absorption and consequent toxic action. Employed on tampons thigenol is indicated in subacute inflammatory uterine conditions. The large, congested uterus diminishes in size under its application, the hemorrhages cease, and normal menstrual function becomes established. Perhaps the best effects of this drug are achieved in inflammations of the adnexa, parametritis and perimetritis. The author uses in these conditions tampons of equal parts of thigenol and glycerin and states that rapid cessation of the pain and absorption of the exudate result. Thigenol is valuable also in gonorrhœal inflammations of the urethra and paraurethral glands. Here it may be used pure on small tampons of cotton inserted just after micturition or it may be introduced into the glands through a platinum needle.—*Revue de thérapeutique*, 1904, No. 24, p. 834.

**Antiseptic Treatment of Middle-ear Suppuration.**—DR. HEINRICH NEUMANN considers that the oxygen liberated by hydrogen dioxide will destroy the anaërobic micro-organisms which exist in old suppurative conditions, but will not affect aërobic bacteria in the same way. Consequently he combines hydrogen dioxide with potassium permanganate. The combination possesses not only the catalytic power of the latter substance, but also its coagulating and oxygenating effect. The mixture gives off a large amount of oxygen and the evolution takes place slowly; consequently its action on the bacteria is prolonged. In tympanic perforations of large size the author proceeds as follows: The canal is cleansed by antiseptic irrigations and then filled with a warm solution of potassium permanganate (1 per cent.). This is allowed to remain for a few minutes, is then removed and the canal is filled with 3 per cent. hydrogen dioxide, which is permitted to exert its action for six to eight minutes. This treatment has achieved remarkable result in otorrhœas of obstinate type.—*Wiener medizinische Presse*, 1904, No. 46, p. 2181.

**Radium in Joint Affections.**—M. SOUPAULT has obtained excellent results from the emanations of radium in subacute joint affections. He reports patients affected with double hydrarthrosis, subacute gono-



coccal arthritis of wrist and hand, subacute articular rheumatism and subacute gout due to plumbism as cured by this means. In acute cases the author met with no success with the radium.—*La presse médicale*, 1904, No. 92, p. 734.

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**Neuronal.**—Chemically this hypnotic is bromodiethylacetamide, a white, crystalline powder slightly soluble in water, easily soluble in alcohol, and resembling menthol in taste, with the addition of slight bitterness. According to Siebert, Becker, and others it produces a quiet slumber about one-half hour after its administration, with no unpleasant after-effects. The drug seems to have no cumulative action and its dosage in mild insomnia is  $7\frac{1}{2}$  grains, in more obstinate cases from 20 to 30 grains.—*Therapeutische Monatshefte*, 1904, No. 11, p. 591.

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**The Action of Digitalis in Combination with Caffeine.**—DR. LUDWIG BRAUN states that the simultaneous administration of digitalis and caffeine has an especially good effect in mitral stenosis, in cardiac disease with symptoms of heart weakness, in aortic lesions, and in arteriosclerosis complicated with aortic insufficiency. The author has studied the effects of these drugs, both separately and in combination, upon the heart and coronary arteries of mammals, and believes that when they are given simultaneously the vasoconstrictor effect of the digitalis is not produced and the action of the heart is favorably influenced. Consequently the favorable action of the combination is attributed to the improvement produced in the coronary circulation. In effect, the only disadvantage of digitalis, its vasoconstrictor action, is obviated by the combination with caffeine, for, in spite of the increase in arterial pressure produced by the digitalis, the coronary arteries remain widely open, and the conditions for plentiful nutrition of the heart remain favorable. The experiments upon animals are borne out by clinical experience, which proves that the effects of the combination of digitalis and caffeine are not produced by either drug alone.—*La semaine médicale*, 1904, No. 47, p. 383.

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**Pyrogallic Acid in Cystitis.**—M. F. MINET reports good results from the use of this agent in tuberculous cystitis. His observations are based on 60 cases, and he recommends the drug in all forms of this condition, both primary and secondary, except that attended by hemorrhage. The technique is simple, and consists in the instillation of 75 drops of a 1:50 to 1:20 aqueous solution. If retention exists the bladder should first be emptied. Local treatment, according to the author, is less necessary in young patients who are able to take a prolonged rest and fresh-air cure.—*Le progres médicale*, 1904, No. 47, p. 420.

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**Hydrotherapy and Tetanus.**—DR. J. SADGER discusses a method of hydrotherapy in tetanus simpler and easier to carry out without the help of assistants than the Freissnitz process. The four steps in his procedure are as follows: (1) a dry pack until sweating sets in; (2) a cool bath with pouring of cold water over the patient, especially over the spine; (3) a wet pack, and (4) the process described under (2) repeated. He cites an instance in which this treatment was used

successfully where the symptoms, including a relapse, were so severe as to lead one to expect a fatal outcome. Other authorities have called attention to the value of cold water in this disease, which is allowed to fall from a height upon the patient. But the commoner methods have consisted in the use of heat. However, by combining both these agents one obtains a favorable result in the condition of the nervous system and in increased perspiration. Also one finds improvement in the patient's general condition, in the relief of cramps, and in the elimination of the toxins.—*Zentralblatt f. die gesammte Therapie*, 1904, No. 11, p. 565.

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## OBSTETRICS.

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UNDER THE CHARGE OF

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**Spontaneous Rupture of the Uterus during Pregnancy through the Scar of the Cæsarean Wound.**—KERR (*Journal of Obstetrics and Gynecology of the British Empire*, November, 1904) reports the case of a patient in her fourth pregnancy, on whom he had two years previously performed Cæsarean section. The first two pregnancies had been terminated by the birth of dead children, and the pelvis was contracted. Cæsarean section was done, and the fundal incision of Fritsch was employed. The child weighed eight pounds, was readily extracted, and the uterine wound closed with little trouble. The patient made a good recovery.

She returned to the hospital in the thirty-seventh week of her fourth pregnancy for a second section. She was in good condition, the abdomen irregularly enlarged, the greater swelling on the right side. The scar of the previous operation was firm, fetal movements were active, the heart sounds not heard, and the cervix admitted one finger, but was not shortened. On admission the patient received an enema and had some abdominal discomfort. She, however, slept. In the early morning a bloody discharge from the vagina was noticed, with slight pain in the right iliac region. The pulse was normal and the temperature slightly below the average. There was no sickness or vomiting, but pain had spread over the entire abdomen. The abdomen gradually became tender; although the pulse remained good until after several hours, the temperature was subnormal, the breathing rapid, the abdomen tender, and the pulse 90. On placing the hand above the abdomen, the foetus could be felt with abnormal plainness. Two tumors could be distinguished, and at the sides of the abdomen there was slight dulness on percussion. On vaginal examination no presenting part could be felt, but the finger was blood-stained.

When the abdomen was opened a large quantity of dark blood escaped

and the membranes and placenta were found intact. The uterus was retracted behind and downward toward the pelvis. The membranes were opened and a fully developed dead child removed. On examination a transverse rupture of the uterus through the scar of the previous incision was present. Supravaginal hysterectomy was performed, and the patient made a good recovery.

In diagnosing the rupture the symptoms were so slight that it was thought that the rupture was incomplete and limited by adhesions. At operation it was found that there were but two slight adhesions, one to the omentum and one to the abdominal wall.

Kerr believes that a scar through the fundus is more apt to give way than the ordinary longitudinal one. The anterior incision is better. On one occasion, on performing a second operation, he found the old cicatrix at the fundus much thinner than other portions of the uterus.

Another feature which predisposed to rupture of the scar was the fact that at the first operation the placenta had been attached at this point. Further, in the second pregnancy the placenta was situated over the scar.

As regards the result of the operation in general, Kerr states that he has now had 30 cases with 2 deaths, a mortality of 6.6 per cent. He has had two repeated Cæsarean sections with good results. He adds the report of 5 cases in which the scar ruptured in a pregnancy following that terminated by Cæsarean section.

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**Two Cæsarean Sections for Eclampsia.**—In the *Zentralblatt für Gynäkologie*, 1904, No. 45, WANNER reports 2 cases of Cæsarean section for eclampsia. In both patients the convulsions were exceedingly severe. The patients were from eight to fourteen days before term, and there was no sign of uterine contractions.

The first patient was a primipara with almost total suppression of urine, rapid pulse, and temperature slightly raised. The cervix was not softened or dilated. Abdominal Cæsarean section permitted the delivery of a living, well-developed male child. The patient died forty-eight hours after operation, with œdema of the lungs.

The second case was that of a primipara, greatly asphyxiated, with rapid pulse and profoundly comatose. The head was freely movable above the pelvic brim, the cervix tightly closed, and there were no uterine contractions. Vaginal Cæsarean section was performed by making an incision through the vulva and perineum on the right side, opening the cervix with scissors upon one side, and then splitting the cervix on the anterior and posterior wall to the internal os. Version was performed and a living, vigorous child extracted. The placenta was removed by expression with free bleeding. The uterus was pressed down, the cervix seized with forceps, and the incisions closed with catgut. After delivery the patient had one convulsion. Four hours after delivery there was hemorrhage, which rendered tamponing of the uterus necessary. The patient also received the injection of salines. On the following day the tampons were removed and the incision in the perineum and pelvic floor closed. The patient remained partly comatose for three days, but finally recovered.

In the vaginal operation incision through the pelvic floor and vulva was made to avoid the necessity of pushing back the bladder from the anterior uterine wall.

**Carcinoma of the Cervix Complicating Pregnancy and Labor.**—In the *British Medical Journal*, November 12, 1904, KERR describes 2 cases of carcinoma of the cervix complicating pregnancy. He states that in the Glasgow Maternity Hospital, they have had, in addition, 4 inoperable cases during the last ten years.

The first case was a multipara, whose first symptom of malignant disease was severe hemorrhage. When seen she was far advanced in pregnancy, and the carcinoma had involved the entire cervix. When admitted to the hospital, no enlargement of the lymphatic glands could be made out. The pregnancy was nearly at term; the heart and lungs were normal. The patient was delivered by Cæsarean section, and a living healthy male child was extracted. The uterus was opened by incision across the fundus to facilitate its complete removal. After emptying the uterus the operator removed it down to the cervix, but the cervix and surrounding tissues were so involved that its removal was impossible. The stump was closed by layers of peritoneum. The patient made a good recovery from the operation, leaving the hospital thirty-three days afterward. She died six weeks after returning home.

The second case was also a multipara in the thirty-eighth week of gestation. Masses were felt upon both lips of the cervix in this case, and there was partial dilatation. Uterine contractions came on and operation was performed.

The cervix was first amputated through the vagina and both uterine arteries were tied. The vagina was then thoroughly cleansed, the hands again sterilized, and Cæsarean section performed by abdominal incision. The child was removed, slightly asphyxiated, but revived. The remainder of the uterus was removed through the abdomen, and the vaginal vault was closed. The patient died on the fifth day after operation, from septic peritonitis.

These cases are types of the two general classes into which they may be divided; first are the inoperable cases, in which Cæsarean section was performed to save the life of the child without the attempt to completely remove the cancer; the second was an example of an operable case, and illustrates the dangers of the operation at the time when pregnancy has nearly reached full term. In dealing with inoperable cases, it is of the greatest importance that Cæsarean section should be performed before labor has begun. The uterus, to prevent infection, should be removed, and the stump treated by careful closure of the peritoneum to prevent infection. In operable cases the uterus may be removed through the vagina as late as the fourth month of gestation. After that the most satisfactory method consists in performing Cæsarean section, after which supravaginal amputation is practised, followed by the removal of the cervix through the vagina. This avoids the risk of contaminating the peritoneum by bringing the cancer through the abdomen. By downward traction the malignant growth is removed from below.

**Lumbar Puncture in Eclampsia.**—In the *Zentralblatt für Gynäkologie*, 1904, No. 45, HENKEL gives the results of 16 cases of eclampsia in Ohlshausen's clinic in Berlin, in which lumbar puncture with extraction of cerebrospinal fluid was performed. These cases illustrated well different types of eclampsia. Some occurred in primiparæ, others in multiparæ soon after labor, and some in the early stages or very beginning of labor. In a considerable number lumbar puncture was per-

formed and fluid extracted, followed by the injection of cocaine and scopolamine.

In some cases the quantity of cerebrospinal fluid was found increased; in others diminished. In some there seemed to be no fluid present, and in others the quantity of fluid seemed normal. The mortality was 25 per cent. This is no improvement on the average mortality of eclampsia under hospital treatment.

So far as these experiments give information concerning the increase of cerebrospinal fluid in eclampsia, in 7 of these patients the spinal canal was empty, and 1 of these patients died; in 5 cases very little cerebrospinal fluid escaped, and 2 of these patients died. In 4 cases the quantity of cerebrospinal fluid was greatly increased, and 1 of these cases died. From this series of cases no practical result whatever followed lumbar puncture and the use of cocaine and scopolamine by injection.

KLEINWÄCHTER (*Zentralblatt für Gynäkologie*, 1904, No. 45) reports a case of eclampsia in which lumbar puncture was employed. The patient had fifteen convulsions, was deeply comatose and greatly prostrated. She had been given chloral hydrate, diaphoretics, thyroid extract, croton oil, and injections of saline fluid into the bowel. Salt solution was also injected beneath the skin and lumbar puncture was employed. One and a half drachms of cerebrospinal fluid was allowed to escape. The fluid escaped in a small stream and not in drops. Cocaine was injected, and salt solution was also introduced into the bowel. The patient improved and was subsequently treated by thyroid extract, sulphate of magnesium, and iron. She ultimately recovered.

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## GYNECOLOGY.

UNDER THE CHARGE OF

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**Endometritis Following Gonorrhœal Vulvovaginitis in Children.**—JUNG (*Zentralblatt für Gynäkologie*, No. 33, 1904) concludes a clinical study of this subject with the following statements: 1. In most cases of vulvovaginitis careful examination of the cervical secretion is usually sufficient. 2. The removal of mucus from the portio on a swab is not enough for diagnostic purposes. 3. The writer's observations, as well as those of Gassmann and Buscke, prove that while gonorrhœal endometritis does occur as a complication of infantile vulvovaginitis, it is infrequent (10 per cent.), while disease of the annexa is very rare. 4. The cervical secretion should be examined bacteriologically in every case of vaginitis in children, especially when it is of long standing. 5. It is doubtful if it is advisable to apply the treatment directly to the cervical canal.

**Styptol in Uterine Hemorrhage.**—WITTBAUER (*Zentralblatt für Gynäkologie*, No. 33, 1904) has used this drug in a number of cases, and concludes that its action is similar to that of stypticin in cases of menorrhagia, and especially in climacteric bleeding, though it is apparently more effective. It does not take the place of ergotin, however, in cases in which it is desirable to cause uterine contractions. Styptol is harmless and is much cheaper than stypticin, and is therefore applicable to hospital and dispensary use.

**Microscopic Diagnosis of Abortion.**—HITSCHMANN (*Zentralblatt für Gynäkologie*, No. 32, 1904), referring to Opitz's conclusions that characteristic glands are always found in tissue removed from the pregnant uterus, describes the same typical glands which he found in scrapings from non-gravid uteri. These are distinguished by the presence of small papillary projections into the lumen of the gland, covered with epithelium, an appearance also noted in the writer's specimens. He concludes that the swelling of the uterine mucosa during menstruation may cause the same peculiar change in the glands as nidation.

**Tubal Menstruation.**—THORN (*Zentralblatt für Gynäkologie*, No. 32, 1904), after discussing this subject at some length and citing two cases from his own practice, arrives at the conclusion that there may occur rarely a sort of vicarious hemorrhage from the tubal mucous membrane. In both of his cases the tubes were diseased, and he holds that this was probably true in every instance in which this phenomenon was noted. At any rate, he denies the occurrence of a normal tubal menstruation as claimed by some authors. Doubtless the healthy tube shares in the general menstrual congestion, but no more.

**Premature Menopause.**—SIREDY (*Zentralblatt für Gynäkologie*, No. 32, 1904) reports five cases in which climacteric symptoms were wanting. In all menstruation began late and was always scanty. The writer attributed the condition to imperfect development of the sexual organs, as evidenced by atrophy of the cervix uteri.

Hartmann (*ibid.*) reports a similar case in a healthy girl, aged nineteen years, whose periods had been regular for four years.

**Etiology of Kraurosis Vulvæ.**—JUNG (*Zeitschrift für Geb. und Gyn.*, Band lii., Heft 1) believes, from the study of several cases, that kraurosis is only an advanced stage of chronic vulvitis, since there is no difference in their macroscopic appearance or clinical symptoms. The histological difference is quantitative rather than qualitative. Kraurosis is not to be regarded as a separate disease.

**Parotitis Following Curettement.**—CONDAMIN (*Lyon méd.*, April 12, 1904) reports a case of parotitis after aseptic curettement, and infers that this complication of gynecological operations is not necessarily of infectious origin, but may be due to reflex nerve irritation through the medium of the sympathetic and cervical ganglia. Thirst after laparotomy may be referred to the same cause—diminution or suspension of the salivary secretion. The invasion of the glands by microbes from the mouth may also play a part; hence the writer

recommends the use of a mouth-wash for a few days after operation, or even the administration of pilocarpine.

**Malignant Degeneration of Ovarian Cysts.**—BARNSEY (*Annales de gyn. et d'obstétrique*, No. 8, 1904) found malignant degeneration in 36 per cent. of his cases. He believes that ovarian cystomata are nearly always benign at first, the cancerous condition being secondary. In 32 operations only one patient died. Recurrence took place in 6 cases, in 5 of which rupture of the cyst occurred spontaneously or during operation. The writer thinks that a cyst which is suspected to be cancerous should be removed entire without previous puncture.

**Shortening of the Round Ligaments.**—DOLERIS (*La Gynécologie*, August, 1904) concludes an article on this subject as follows: 1. Fixation of the uterus is an unphysiological operation, depending for its success on pathological conditions; indirect, or ligamentary, hysteropexy is always preferable. 2. Operations for fixation of the organ are not unattended with risk and the ultimate results are uncertain. 3. From an obstetrical point of view extraperitoneal or intraperitoneal shortening of the round ligaments is much safer, as shown in 177 cases collected by the writer in which there was no instance of dystocia. 4. These operations meet all indications, whether the case is simple or complicated. 5. It is not enough to retain the uterus in its normal position; plastic operations on the cervix and pelvic floor must not be omitted when indicated.

**Foreign Body in the Vagina.**—ORLOY (*Roussky Wratsch; La Gynécologie*, August, 1904) reports the case of a peasant woman, aged sixty-six years, who entered the hospital with pain in the lower abdomen and a foul discharge. She stated that thirty years before, after the birth of her child, she had procidentia, which was aggravated after a second confinement. In order to keep the uterus in position she had introduced into the vagina a croquet ball, which gave entire relief and had not been removed since. On examination the ball was found to be so firmly impacted, on account of the senile atrophy of the tissues, that it was necessary to remove it piecemeal. A few areas of ulcerations were present, which healed in a few days.

**Gonorrhœal Inflammation of Skene's Glands.**—POLLAK (*Zentralblatt für Gynäkologie*, No. 9, 1904) found the glands involved in 45 out of 100 cases of subacute and chronic gonorrhœa in which the diagnosis was confirmed by bacteriological examinations. In 31 cases only one gland was involved. The writer concluded that there was no relation between the number of gonococci found in the urethra and those in the glands.

**Paralysis after Narcosis.**—GLITSCH (*Zentralblatt für Gynäkologie*, 1904, No. 39) thinks that this accident is due to several causes, viz.: 1. Forced elevation of the arms and simultaneous rotation outward, causing pressure of the clavicle against the first rib and consequent involvement of the brachial plexus. 2. When the capsule of the shoul-

der-joint is opened in the cadaver, so that the head of the humerus can slip forward, this pressure is absent. 3. Under the same conditions with the arm raised above the horizontal, the head of the humerus presses on the plexus.

The writer infers that clinically postoperative paralysis results from temporary pressure of the head on the infraclavicular portion of the plexus, due to hyperelevation of the arm, with rotation inward. He accordingly favors Holst's method of securing the arms at the sides, resting on cushions. Attention is called to the medico-legal importance of the lesion.

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**Benign Chorioepithelioma.**—VELITS (*Zeitschrift für Geb. u. Gyn.*, Band lii., Heft 2) describes the case of a multipara, aged thirty-four years, who, a month after the excision of a vesicular mole, began to have uterine hemorrhages. A growth was removed, which was pronounced to be chorioepithelioma. The uterus was extirpated and the patient had remained well for a year.

From a study of this one and other specimens the writer concludes that spontaneous cure of these neoplasms may occur through necrobiosis, as shown by the lowered vitality and disappearance of the cells of Langhans and the appearance of wandering cells, which show the separation of the syncytium.

HAMMERSCHLAG (*ibid.*) reports only 4 cases of chorioepithelioma from the Königsberg clinic among 5000 gynecological cases, to which he adds a fifth. The patient's ages ranged from thirty-two to forty-seven years, and all had borne at least seven children. The neoplasm developed each time after a previous abortion; three after molar pregnancy, the time varying from five weeks to two and a quarter years. Three died, two being cured by vaginal extirpation. The ovaries were all diseased, usually showing cystic degeneration.

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**Physiological Studies of the Uterus.**—FRANZ (*Zentralblatt für Gynäkologie*, 1904, No. 24) presents the following deductions regarding the uterine muscle, based on a series of experiments with rabbits as well as with human uteri examined immediately after removal: 1. In rabbits the uterus can always be excited to contract by mechanical or electric stimulation. 2. When drawn out of the abdominal cavity in the living animal and suspended it contracts spontaneously, possibly from a lowering of the temperature. 3. The virgin organ is less susceptible to stimulation than the nulliparous, and the pregnant most of all. 4. When removed from the body the uterus in the rabbit responds but slightly to electric stimulation, even when freshly excised. 5. The organ responds most vigorously to thermic stimulation (immersion in salt solution at a temperature of from 50° to 60° C.), but the muscle soon becomes relaxed. Low temperatures (0° to 5° C.) cause contractions, which increase gradually and persist for a long time. 6. A series of rhythmic contractions can be produced by electric stimulation. 7. There is no marked difference between the muscular irritability of the freshly excised uterus in the rabbit and human female, except that there is a weaker response in the latter to electric reaction, thermic stimulation having the most marked effect, even in atrophic post-climacteric uteri. 8. The freshly excised vagina in the rabbit shows a similar response to



stimuli, especially to thermic, when the contractions become rhythmical. 9. Chloral hydrate prevent the contractions in a uterus suspended *in situ*, ergotin increases the muscular irritability and tendency to rhythmical contractions, atropin has a negative effect, while nicotin produces strong tetanic contraction.

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## OTOLOGY.

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**A Contribution to the Pathology and Pathological Anatomy of Congenital Deaf-mutism.**—G. ALEXANDER (*Archiv. f. Ohrenheilkunde* Band lxi., Heft 3) reports the pathology of an interesting case of congenital deaf-mutism. The deaf-mute, who, for a long time, had been an inmate of a poor-house in his native town in lower Austria, came to Vienna and sought work. He was employed variously and had no symptoms of any disturbance of equilibrium until finally, being engaged on work on a scaffolding a few metres high, he fell and suffered an injury to his urethra (rupture of the urethra). This injury was followed by pyæmia, of which he died. The organs of hearing were obtained and showed the following pathological conditions:

1. The static labyrinth: The nerve branches and the vestibular ganglia were atrophied, and the nerve terminations showed a corresponding degree of atrophy. The neuroepithelium was found to be lower than normal and showed an evident diminution in the number of sense cells and a relative increase in the number of supporting cells. The cupulæ in the ampullæ were smaller in size than the normal and, in utriculus and sacculus, the otolith membranes and the otoliths were also smaller. The epithelial lining of the static labyrinth, aside from the neuroepithelium, was, for the most part, normal, but here and there there were diffuse or circumscribed thickenings. In places there were epithelium-lined cysts arising from the epithelial layer and projecting into either the endolymphatic or perilymphatic lumina. The whole static labyrinth and its connective nerve branches and ganglia were markedly anæmic and free from pigment. The ductus endolymphaticus, the utriculosaccular canal, and the ductus reuniens were normal. The bony capsule of the static labyrinth was normal.

2. The acoustic labyrinth: The cochlear nerve presented in its entire course an evident atrophy (about one-third of the normal), and its ganglion showed a corresponding atrophy. The grade of atrophy (hypoplasia) was not the same in all places, but varied with that found in the corresponding level of the peripheral endings. The spiral ganglion was found very different from the normal (a spiral course

being evident only at the beginning and in the basal turn). From the end of the basal turn upward the ganglion was represented only by a heap of cells which was situated in the axial part of the cochlea. From this it resulted that the peripheral nerve fibres of the middle and apical turns of the cochlea were much longer than the normal.

The osseous cochlea, considered in its bearings on the pathology of congenital deafness, presented a most interesting condition. While the outer wall, except for the fact that the end of the middle turn and the apical were a little decreased in height, was normal, the whole bony tissue of the modiolus and the lamina spiralis ossea, from the level of the middle turn upward, was wanting. Likewise, in the vestibular division and in the basal turn, the lamina spiralis ossea secundaria was wanting. This failure of the bony modiolus had as a result in the region above the beginning of the middle turn that the scala vestibuli of one turn formed with the scala tympani of the next turn a common space. The helicotrema was wanting and the membranous apical turn closed off the cupola completely below. The ganglion found in the cochlea and its peripheral fibres were quite surrounded in a mass of connective tissue, and in place of the lamina spiralis ossea there were fibrous plates between which ran the atrophic nerve branches.

The membrana basilaris was found in some places particularly thick, in others, thinned. The epithelium on the surface of the membrane directed toward the tympanic scala was, for the most part, present. The spiral vessel was lacking in many places entirely. The crista spiralis was for the most part flattened out and its substantia propria was lacking. Here and there in the crista were cysts lined with epithelium and containing a homogeneous substance. The membrane of Corti was, in the altered middle and apical turns of the cochlea, in its normal position, but in places it was found in the sulcus spiralis internus, rolled up and surrounded by an epithelial border. The epithelium, which here surrounded it was continuous with that of the sulcus spiralis internus. The papilla basilaris was absolutely normal in no situation. In the lower part it was entirely wanting. In other parts, *e. g.*, in the upper turns, it was evidently in an embryological stage, consisting of several rows of epithelium, showing neither differentiated hair cells nor rods. However, many of the cells presented projecting hairs which were in contact with the altered membrane of Corti. In places, the rods of Corti were present intact, and in others, in a rudimentary condition. In the papilla itself, the typical hair cells were wanting throughout. The ligamentum spirale showed, where the membranous canal was preserved, the normal form. In its structure it was in places of a richer cell structure, and in others, the cell elements were few in number. The stria vascularis showed a varied condition. In places entirely wanting, in others it was replaced with pavement epithelium alternating with cylindrical epithelium. The connective tissue of the stria was sharply divided from the epithelium, showing nowhere the characteristic intimate union. The vas prominens was only in a few places evident, and, indeed, the whole cochlea was poorly supplied with bloodvessels.

Alexander regards the condition of the cochlea as evidently a result of arrested embryological development, and finds that an analogous condition obtains in the human embryo at the age of two to three months. As to the condition in the static labyrinth, Alexander has found a

similar condition in the static labyrinth of the dancing-mouse. The dancing-mouse has been found, in experiments conducted by Kreidl and Alexander, to be unable to walk on a narrow support for any distance, although, in ordinary walking, it shows no disturbance of equilibrium. He, therefore, suggests that here in this case we have a physiological analogy. In ordinary occupations, this deaf-mute showed no disturbance of equilibrium. Only when engaged on work on a narrow staging did this faulty equilibration become evident, leading to the deaf-mute's fall and injury which was followed by his death.

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**Epileptiform Convulsions in a Case of Chronic Suppurative Middle-ear Disease; Recovery Following Mastoid Operation and Lumbar Puncture.**

—HUBER (*Annals of Otology*, April, 1904) presents the following case:

The patient, a child aged two and a half years, had a history of adenoids and of a fetid discharge, from the right ear, of two years' duration.

For a period of two weeks preceding examination the child had been restless, crying a great deal, and finally, shortly before the date of the examination, had a convulsive attack lasting from two to three minutes; these attacks were repeated, sometimes at half-hour intervals, occasionally accompanied by vomiting, and occurred impartially by day or by night, apparently without extraneous exciting cause.

On examination the child was apathetic, in a half comatose condition; the extremities were cold and cyanotic; there was convergent strabismus, slight horizontal nystagmus, dilated pupils, the right pupil especially; *tâche cérébrale*; a pulse of 130, but regular; a temperature of 100°, and exaggerated reflexes.

In the right ear there was a large perforation of the drumhead, through which flowed a copious stream of offensive pus.

Passive movements excited general muscular contraction, and a lumbar puncture was done, with the result of a cessation of this reaction.

The postaural operation revealed a pus cavity with bulging dura, and, on two successive days after operation, the lumbar puncture was repeated and followed by a diminution and then a disappearance of the general symptoms.

On the twenty-second day after operation the child was apparently well and was discharged from treatment.

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**Bone Conduction and the Sound-transmitting Apparatus of the Middle Ear.**—In this continuation of his series of experimental investigations BEZOLD (*Zeitschrift f. Ohrenheilkunde*, Band xlviii.) comes to the conclusion that, with both ears firmly closed, while sound waves conveyed through the medium of the air are not perceived, and while, on the contrary, sound waves conveyed to the head by direct contact with the sounding body are distinctly heard, by bone conduction, in all probability only such sound waves are perceived, in the latter instance, as pass to the percipient organ through the medium of the sound-transmitting apparatus, and such, moreover, as set the sound-transmitting apparatus, and the column of intralabyrinthine fluid equally, in transverse vibration.

The author further concludes, from theoretical deduction based upon his observations, that it is only the transverse translation of the to-and-

fro movements of the membrana basilaris, by its sympathetic vibrating mechanism, that actuates the cells of the organ of Corti, and that the role, in the function of hearing, of the sound-transmitting apparatus consists in the conversion of the longitudinal waves, transmitted through the air or conveyed by bone conduction, into transverse vibrations.

**Diseases of the Ear in the Italian, French, German, and Austro-Hungarian Armies.**—G. OSTINO (*Centralblatt für Ohrenheilkunde*, ii., 8) gives a general review of this subject, based upon army statistics, which must of necessity be subject to difficulties because of lack of uniformity in records as well as differences in rules determining leave of absence and discharge from service; but the mass of material at command gives the statistical review a value for purposes of comparison with similar statistics in civil life.

The exclusion from service of from 1.5 per cent. to 2.4 per cent. of recruits on preliminary physical examination, on account of active diseases of the ear or because of resulting impairment of hearing, serves to decrease the percentage of soldiers who would otherwise be suspended or discharged from service on the same account, and tends to explain the low percentages given.

A comparative study of these statistics is also valuable as throwing light upon the differences in the limitation of the medical examination, as, for instance, in the year 1897 the number of men discharged from service in the Italian army was 1.5 per cent.; the French, 0.93 per cent.; the Prussian, 1.85 per cent., and the Austro-Hungarian, 4 per cent., the reason for the larger last-named percentage being the fact that both monaural deafness and the existence of a dry perforation of the drumhead are sufficient considered reasons for rejection or for discharge from the Austro-Hungarian service.

This question of the influence of a dry perforation upon the estimation of serviceableness has long been a matter of controversy among military surgeons. Eichbaum (*Deutsche Militarärztliche Zeitschrift*, 1889) is of the opinion that cases of this kind may be admitted to or retained in service, the causative suppurative process having ceased; unless the perforation is large, half or more of the drumhead; unless there is perforation of the membrane of Shrapnell; unless there are granulations in the middle ear, or if there is also chronic nasopharyngeal catarrh or constitutional disease. Schwartz (*ibid.*, 1900) attaches no importance to the size of the perforation, but considers especially the cause of the aural disease, its duration, the general condition of the patient, and whether both ears are affected or only one.

Scholze (*ibid.*, 1901) is of Hartmann's opinion, that if, after a suppurative cause, there is a persistent opening in the drumhead, with the mucous membrane of the tympanic cavity dry and dermoid in character, there is but slight danger of recurrence, and that such cases are not only admissible to service, but should be made the subjects of treatment in view of the considerable possibility of further bettering their condition. Villaret (*ibid.*, 1899, 1900), as the result of consecutive statistics, proved a considerable increase of ear disease among the soldiers during the months when they practised swimming, and commented critically upon the order that "persistent perforation of the drumhead is no longer to be regarded as reason for rejection or discharge."

Of 321 cases of this kind in the Austro-Hungarian army, 23 only were subsequently admitted to the hospital on account of a recurrence of the suppurative process, the remaining 298 finishing their service without going upon the sick list, although 26 out of that number had some degree of suppuration in the middle ear, these statistics differing considerably from those of Scholze, who found at the military station in Mainz 20.7 per cent., and at the station in Muhlhausen 22.7 per cent. of recurrences of suppurative middle-ear disease.

To the value of statistical research uniformity of statement is most important, and that this does not pertain in the statistical study in question is evident when the different forms of aural disease are taken into consideration, for in the Italian and French statistics no distinction as to the part of the ear affected is made, while the German statistics differentiate between "diseases of the outer ear, including the drum-head," and "diseases of the middle and inner ears, including deafness." The percentage of relationship cases under these two headings in a period of fifteen years—1874 to 1889—was 74.1 per cent. of the former and 25.9 per cent. of the latter, the preponderance of the former being due not only to the greater liability to injuries of the external ear in military service, but also to the fact of the classification of the drum-head as a part of the external, when, properly, it belongs to the middle ear.

Comparative statistical conclusions are rendered difficult, also, not only by the difference in construction of terms in the different services, but by the changes in the quality of material at different times with the influx of new recruits and the changes of station.

As concerns the period of the year in which aural diseases especially prevail, this is influenced by the increase in the number of new recruits as well as by climatic change. For instance, in the Italian army the percentage of ear diseases is higher in March and April, because of the prevalence among the troops of measles and influenza, and higher in January, because of climatic conditions and the influx of cavalry recruits. In the Austro-Hungarian army the percentage increase occurred in the same months for nearly the same reasons, while in the Prussian army the major percentage occurred in July—a circumstance which leads Villaret to infer that this increase is due to the prevalence of swimming and to the effects of the spring field manoeuvres, a view scouted by Scholze, who draws attention to the fact that the percentage was less by 0.03 in the three summer than in the three winter months, and that it may, therefore, be not unjustly concluded that the weather had a more prejudicial influence upon the ears of the troops than either swimming, the detonation of fire-arms, or the inhalation of the dust of country roads.

As regards the liability of the different branches of the service, that which was true of the Italian army—a greater percentage of ear disease among the infantry—was measurably true of the other armies here considered, but the French statistics show a very considerable preponderance of ear diseases, as high as 5.9 per cent. among the troops on foreign service and especially in the tropics—a condition with which our own service is not unacquainted in the Philippines.

# OPHTHALMOLOGY.

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UNDER THE CHARGE OF

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**A Common Misconception of Astigmatic Refraction.**—SUTER (*Annals of Ophthalmology*, January, 1905) calls attention to a misconception which we suppose almost every student of refraction has at some time held, and from which many never free themselves. The error is the more widespread from the fact that some text-books actually teach it, and others do not make the matter as clear as it should be. The error is this: that in astigmatism the meridians intermediate between the two principal meridians have each a separate focus, which is situated upon the optic axis somewhere between the focus for the meridian of least curvature and the focus for the meridian of greatest curvature. As a matter of fact there are but two foci upon the principal axis—one for the meridian of least curvature, and one for that of greatest curvature.

The focal lines are two lines perpendicular to the axis at each of the foci, anterior and posterior; the directions of the two lines are at right angles to each other, being parallel respectively to the principal meridian to which each belongs. A pencil of parallel rays refracted by an astigmatic surface is divided into two pencils, one of which is brought to a focus at a point in the anterior focal line, and the other at a point in the posterior focal line. Thus of two rays impinging upon opposite extremities of an intermediate meridian, neither will ever meet the optic axis nor will the two rays meet each other, and, consequently, there can be no focus for rays lying in this meridian.

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**The Operative Treatment of High Myopia.**—FROST (*Brit. Med. Jour.*, November 12, 1904) details his experience and conclusions based upon operations on 39 eyes in 35 patients during the past nine years. The patients' ages ranged from ten to forty-eight years; 2 were lost by suppuration, rather strangely the only cases under twelve years of age. Detachment of the retina occurred in 8 cases, but it is difficult to say that this event was due in every case to the operation; thus in 1 case the detachment did not occur until six years after the operation; in another the interval was four years; in 2 two years; in 3 others it was eight months, four and two months respectively, and in 1 ten weeks. The result was vitiated in several other cases by chronic disease, such as cyclitis, glaucoma, and choroiditis. As regards the degree of myopia, the writer's view is that the operation is of little benefit if the resulting ametropia exceeds 4 D. This condition is only fulfilled if the myopia is not less than is corrected by a lens of  $-15$  D. placed 10 mm. in

front of the eye. This represents a myopia of only 13 D. measured from the cornea.

The optical effect of removing the lens increases with the degree of myopia; an emmetropic eye rendered aphakic requires about 10.50, whereas an eye myopic 25 D. becomes nearly emmetropic; that is, such an eye would have to be 31.1 mm. in length, and this is the posterior focal distance of the cornea.

The visual acuity also must be taken into account when considering the probable benefit to be derived from the operation. The improvement to be expected therefrom can only be due to increased size of the retinal image, so that when the defective vision before operation is due to fundus changes it is irremediable by the operation. At the same time the changes actually visible with the ophthalmoscope afford a very unsafe guide in forming an opinion as to the improvement that may be obtained after the operation. The writer tests the visual acuity by the ability to read No. 1 Jaeger at the patient's far point. A rough but practically useful test.

The operation is usually called for only in young adults, or at the age of puberty; high myopia in young children is very rare. Young eyes thus affected are probably unsound and bad subjects for operation. Older people do not frequently require the operation, because they have chosen their path in life and have become accustomed to the inconvenience of wearing strong glasses. In the series reported only 5 were over thirty-five years old.

Should both eyes be operated on? When improvement has resulted from the operation on one eye it is rare that the same result is to be expected from the other. There is usually a difference of several dioptries in the myopia of the two eyes. Moreover, operation on the second eye deprives the patient of the ability to see near objects without glasses.

In the discussion which followed this paper, which was read before the section of Ophthalmology of the British Medical Association, Dr. E. Landolt remarked that highly myopic eyes were almost always diseased eyes affected with chronic choroiditis and its multiple consequences. Operation on the weaker of the two eyes would probably not yield a great advantage. Operation on the better eye might lead to entire loss of useful sight. Extraction was admissible only on one of two relatively good eyes of about 20 D. myopia.

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**Posterior Cortical Cataract of Traumatic Origin.**—KOLLER (*Annals of Ophth.*, January, 1905) reports the case of a young man who received a perforating flap wound in the upper outer quadrant of the cornea of equitriangular shape, each side about 3 mm. long. Examination six days later showed that the flap was well adapted. In the region of the posterior pole of the lens a delicate star-like, somewhat diffuse opacity was present. Three and one-half weeks after the injury, the opacity of the posterior pole was smaller but much better defined. Vision was  $\frac{6}{18}$ ; with the stenopæic slit it was  $\frac{6}{12}$ . A better scrutiny of the anterior part of the lens with the ophthalmoscope revealed a condition which had most likely existed from the start, but had escaped notice. In the anterior capsule of the lens exactly corresponding to the inner angle of the corneal wound was an opacity not larger than the finest dot, and adjoining it, outward and downward, the most

anterior layer of the lens showed a delicate, frost-like, bean-shaped opacity, its axis slanting from the nasal to the temporal side. It is now five years since the accident and both opacities are practically unchanged, except that the anterior cortical opacity is larger. The vision with the proper correction is  $\frac{5}{8}$ .

Posterior cortical cataract of traumatic origin appears to be very rare; perhaps this is only apparent, its presence being hidden behind anterior opacities which are so common after perforating injuries to the lens or contusions of the eye.

Posterior polar cataract is to be distinguished from posterior cortical cataract (Fuchs). Posterior polar cataract is a small white dot at the posterior pole outside the lens; it is congenital and due to incomplete involution of the hyaloid artery. Posterior cortical cataract is much larger and shows the structure of the posterior cortex. It is very common in degenerative affections of the deeper structures of the eye, but has been recorded only a very few times as a sequel to traumatism, piercing wound of the lens, or simple contusion of the eye. It is an interesting and puzzling fact that in the case of perforating wounds of the lens the location of the lens wound seems to have no direct relation to the posterior cortical opacity. The opacity develops shortly after the injury and may result in complete cataract. It generally remains stationary after clearing up somewhat in the first weeks. This clearing makes it likely that the cause of the opacity is not destruction or alteration of the lens fibres, but it may be due to some deposit between them which can again disappear.

Various hypotheses have been advanced to explain this curious formation. Fuchs thinks that it is due to a gorging of preformed spaces (lymph spaces) by a liquid. Some observers have supposed that they had demonstrated the existence of such interfibrillar spaces, but recent researches are against the assumption that preformed lymph spaces exist in the normal lens. Zur Nedden assumes that the traumatism leads to momentary displacement of the lens within the capsule with loosening of the lens fibres at the posterior capsule. In consequence of this loosening some fluid from the vitreous enters into the cementing substance between the fibres of the lens. This hypothesis does not explain why this loosening should take place at the very pole of the lens, and why it should be so absolutely symmetrical. Further experiment is necessary to explain this curious and interesting phenomenon of the lens reacting with a change at its posterior pole to injuries inflicted on its anterior surface.

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**An Epidemic of Acute Catarrhal Conjunctivitis Due to the Koch-Weeks' Bacillus.**—SNELL, Sheffield (*Lancet*, August, 13, 1904), reports the occurrence of such an epidemic in a rural district embracing about 12,000 inhabitants. Over 200 individuals were affected. The overwhelming majority occurred in children; in all cases both eyes were affected. The cornea was involved in but a single eye in a woman, ending in perfect recovery. Isolation and appropriate treatment soon put a stop to the outbreak.

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**Congenital Word-blindness.**—HINSHELWOOD, Glasgow (*The Ophthalmoscope*, October, 1904), reports another case, making his fifth of this rare condition. The subject was a boy, aged twelve years, who had



the greatest difficulty in learning to read. While he was unusually bright at figures and an average speller, he could rarely read by sight more than two or three consecutive words, but came to a standstill every second or third word, and was unable to proceed unless he were allowed to spell the word aloud, thus appealing to his auditory memory, or so spell it silently with his lips, thus appealing to his memory of speech movements. His refraction, visual acuity, and fundus were normal.

This defect appears to be due to a difficulty in acquiring and storing up in the brain the visual memories of words and letters. It may not extend beyond this visual group of images. The visual memories of numbers and musical notes may be quite normal. These facts are to be explained by the different groups of visual images being stored up in different, but probably contiguous, areas, most likely the angular gyrus of the left side. As defect of the gyri on both sides is rare, re-education can be accomplished with great perseverance. The obstacle is probably due to the fact that all the centres involved in speech are on the same side of the brain.

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**Glaucoma and the Glaucoma Theories.**—PATTERSON (*Scottish Medical and Surgical Journal*, July, 1904) gives an interesting exposition of the present views upon this subject. The source of the aqueous humor is to be found in the epithelium of the ciliary region. Leber describes the secretion of the aqueous as a transudation or filtration process depending upon a difference of pressure between the blood in the vessels and the fluids in the chambers of the eye. Doubtless, however, the epithelial cells play more than a passing or mechanical role. No direct nervous mechanism has been demonstrated. By acting indirectly through the vasomotor nerves, the balance between blood pressure and intraocular pressure, and, consequently the amount and character of the secretion may be greatly modified. Normal aqueous strongly resembles normal saline solution. After puncture of the anterior chamber it contains much albumin and fibrin and is spontaneously coagulable. The vitreous humor is really a tissue of the finest fibrilles, containing in their meshes a fluid almost identical in composition with the aqueous. This fluid can pass through the zonula, but the interchange of fluid in the meshes of the vitreous is probably very slow.

Almost the only path for the elimination of fluid from the eye, at least in man, is the filtration angle. In addition, there is probably some absorption of fluid by the vessels of the iris and a slow passage from the vitreous by the optic nerve. Schlemm's canal is a venous rather than a lymph sinus. It often contains blood corpuscles. It communicates by the minutest pores with the anterior chamber; the anterior ciliary veins have direct communication with it, so that fluid from the anterior chamber passes directly into the veins of the sclerocorneal margin.

The fluid contents of the eyeball stand at a pressure midway between the arteriocapillary and venous blood pressures. It equals about 25 mm. Hg.; physiological variations from this standard are possible only in a very limited range. The tension is the same in the aqueous and vitreous chambers. This is not altered by accommodation. The intraocular tension can never exceed the blood pressure in the ciliary arteries, 90 to 110 mm. Hg. The blood pressure in the capillaries of the ciliary region has been estimated at about 50 mm. Hg.; that in the veinlets into which the fluid filters from the anterior chamber at about 10 to 15

mm. Hg. Mydriatics and myotics have no influence on the tension of the normal eye. Increase and diminution of the blood pressure have a corresponding effect respectively upon intraocular tension. Division of the sympathetic appears to cause some transient diminution of tension.

*Glaucoma.* Attempts at producing glaucoma in animals have usually succeeded but imperfectly. The most successful was Bentzen, in Leber's laboratory, who produced permanent increased tension by wounding the tissues at the filtration angle, which caused adhesions, shutting of the angle. In secondary glaucoma an evident mechanical obstruction can usually be demonstrated, giving rise to retention.—*e. g.*, fragments of lens matter in traumatic cataract, blocking the spaces of Fontana, etc.

In primary glaucoma these mechanical explanations no longer suffice. A great obstacle in the way of investigation is the difficulty of obtaining glaucomatous eyes for examination in the earlier stages of the disease, of which very few cases have been published. The later lesions are (1) cupping of the disk with accompanying optic atrophy, (2) closure of the filtration angle, (3) degenerative changes in the intraocular bloodvessels. Most of the glaucoma theories stand in close relation to 2 or 3. The older views of glaucoma associated with the names of von Graefe and Donders were based on the idea of hypersecretion. These views have been largely abandoned. A new conception of glaucoma was introduced by Knies. This regards the increased tension as caused by retention due to adhesions of the root of the iris to the cornea, blocking the filtration angle. Weber explained this by forward pressure of the swollen ciliary processes. While the angle is undoubtedly frequently blocked, most observers no longer regard this as a primary lesion, having been found absent in certain glaucomatous eyes examined in the early stage. Czermak and Birnbacher have laid special stress on the diseases of the vertex veins, endophlebitis, and periphlebitis, but this does not appear to be constant. Priestley Smith brought forward a theory which considers the circumlental space as becoming narrowed, especially in hypermetropic eyes, from the growth of the lens. There are many difficulties in the way of accepting this. Panas appears to favor a modified secretion theory due to changes in the nerves and bloodvessels. Abadie's idea that glaucoma is due to disease of the sympathetic has not found much favor.

The author, like most observers, favors a retention theory. One great point in its favor is the well-known fact that glaucomatous eyes remain hard for a long time after enucleation. There is practically no outflow from such eyes. The extreme shallowness of the anterior chamber in glaucoma has never been satisfactorily explained. Injection of fluid into the vitreous in animals' eyes causes very little shallowing of the anterior chamber. In eyes liable to acute glaucoma a very shallow anterior chamber is the rule. With the blocking of the filtration angle, there is probably an advance of the root of the iris and anterior part of the ciliary body, which further increase the shallowness of the anterior chamber.

In explaining the more chronic forms of glaucoma, the writer would lay most stress on changes in the vascular system, both general and local. Signs of vascular degeneration, both local and general, are most marked in the variety which occurs in association with retinal hemorrhage. Being characteristically a disease of advanced life, its relation to changes in the vascular system seems especially noteworthy. Zimmer-

man, in a recent paper, expresses the view that glaucoma depends on a reduction of arterial blood pressure leading to nutritive changes, transudation, etc.; but experiment and clinical evidence seem alike opposed to this opinion. In fact, the writer believes that such patients present an increased rather than a lower arterial pressure.

It does not seem worth while to study further the changes in glaucomatous eyes unless the examination be made in the earlier stages, perhaps such opportunities might be found in animals, as the disease is said to occur frequently in aged dogs kept under highly artificial conditions.

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## PATHOLOGY AND BACTERIOLOGY.

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**The Importance of Bacillus Pneumonia Friedlaender as a Cause of Pneumonia.**—STÜHLERN (*Centr. f. Bak. und Parasitknd.*, 1904, Bd. xxxvi., p. 493) records ten cases of pneumonia in which the bacillus pneumoniae Friedländer was recovered either from the consolidated lung at autopsy or from the sputum during life. In three instances this bacillus was found in the lung unassociated with other organisms. In five cases there was a mixed infection of bacillus pneumoniae and diplococcus lanceolatus, and twice these two organisms, together with staphylococcus pyogenes aureus, were cultivated from the sputum. At autopsy the lungs presented the picture of an atypical lobar or pseudolobar pneumonia, often hemorrhagic in character. The symptomatology and physical signs were those of an atypical lobar pneumonia, bloody, slimy sputum being common. The prognosis is very unfavorable and the mortality high.

**Tuberculosis of the Mitral Valve and of the Aorta.**—Tuberculosis of the heart valves may arise in one of three ways: by direct infection through a deposit of tubercle bacilli upon the endocardium, through hæmatogenous infection by way of the bloodvessels of the valves, and from secondary infection of vegetations or thrombi. WITTE (*Ziegler's Beiträge*, 1904, Bd. xxxvi., p. 192), from a review of the literature, concludes that true tuberculous endocarditis is of extremely rare occurrence, and, eliminating many doubtful cases reported, he would include in the above group only the cases reported by Benda, Burkhardt, and possibly the one recorded by Tripiet. The author describes a tuberculous infection of the mitral valve following a right tuberculous coxitis and accompanied by generalized tuberculosis. There was no chronic valvular disease, no vegetation, and no mixed

infection. The valve was the seat of a conglomerate tubercle having a caseous centre, in which tubercle bacilli were found. The tubercle was situated within the tissue of the valve. Excluding the possibility of a deposit of bacilli upon the endocardium or an extension of the process from the heart muscle, the author concludes that the bacilli reached the valve by way of the vasa vasorum. Besides the above case, two instances of tuberculosis of the aorta are recorded, illustrating two different modes of infection. In one case there was a miliary tuberculosis of the intima associated with generalized miliary tuberculosis. A few small sclerotic areas were seen through the length of the aorta, and it is assumed that one of these offered a point for infection. In the second case the tuberculous process extended from some neighboring lymph nodes through the wall of the vessel toward the lumen. In neither instance could the origin of the generalized tuberculosis be traced to the lesions in the aorta.

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**Report on Trypanosoma and Trypanosomiasis, with Special Reference to Surra in the Philippine Islands.**—MUSGRAVE and CLEGG (*Report of Superintendent of Government Laboratories in the Philippine Islands*, year ending September 1, 1903) contribute an elaborate and excellently illustrated article on the subject of trypanosomiasis. From their work they conclude that trypanosomiasis is a general infection caused by trypanosoma. The term "trypanosomiasis" in a general sense is used to designate all varieties of the infection as found in different animals. A long list of vernacular names now in use, except surra, should be discarded or else allowed to fall simply as synonyms, save in those cases where the infecting parasite is shown to be a species distinct from *Trypanosoma evansi*. The disease is distributed over large areas of the tropical and subtropical world, corresponding closely in its dissemination to the malarial zone. *Trypanosoma* are discussed in general with reference to history, methods of study, general characteristics, including modes of multiplication, agglutination and involution forms, distribution in the body and outside of the body, and the life-cycle of the parasites. The life-cycle is as yet unknown, but it is believed to be acted out entirely within the animal economy. A tentative classification is adopted for purposes of study, and each trypanosoma of importance is discussed with reference to its principal characteristics, habitat, and pathogenesis. Differential diagnosis of trypanosoma of mammals, like the life-cycle, is left an open question, but the authors believe, from a review of the literature and from their own observations, that at least three of the species to which separate names have been given are in reality identical with *Trypanosoma evansi*. The authors draw attention to the spread of the disease through wounded surfaces in which biting insects, particularly flies and fleas, serve as the principal agents. The prevalence of the disease is dependent upon the presence of a host for trypanosoma and the insects for the transmission of the parasites. Animals which serve as hosts for the perpetuation of the disease during the dry season differ in different countries. In Manila sick horses exist in sufficient numbers to carry the infection from one rainy season to another, but it is thought that cows and rats may also aid in its perpetuation. Statements concerning the infection of pastures and water and the transmission of the trypanosoma through sound mucous membrane have nothing to support them. The path-

ology, anatomy, and symptomatology of the infection in various species of animals are discussed. The manner in which the symptoms vary in different animals makes this discussion necessary in order to come to satisfactory conclusions concerning the diagnosis and intelligently to control the epidemics.

A chapter is devoted to the consideration of the identity and individuality of surra, nagana, dourine, and mal de caderas. As in the case of the parasite, the authors have left the subject open, but they are strongly inclined to believe that these diseases are the same, in which case surra would be the only vernacular name allowable. They find nothing in the clinical study of these diseases to differentiate them, and the only real arguments in favor of their individuality are based upon morphologic differences in the parasites. These differences appear so slight that a positive classification could not be founded upon them.

The study of prophylaxis includes the consideration of quarantine laws intended to prevent the infection and reinfection of the country, as the case may be, and the methods for the control and eradication of the disease in territories in which it already has a foothold. In discussing this matter the writers have limited themselves almost entirely to the consideration of means adapted for destroying the hosts and supplemented by those suitable for combating the carrying agents. Prophylactic and curative serumtherapy have thus far failed to give successful results, but if recent reports from Africa are to be trusted preventive inoculation is not entirely without promise of success. All methods tried for the treatment of the disease have been without results, particular importance, or significance.

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**The Pathogenesis of the Crisis in Lobar Pneumonia.**—TCHISTOWITCH, in the *Annales de l'Institut Pasteur*, 1904, May 25, No. 5, continues his work upon pneumococcic infection. He has performed a series of experiments to determine the principal factors involved in the production of the crisis in lobar pneumonia.

In former researches the author has already established that if animals are subjected to a pneumococcic infection of non-fatal severity a leukocytosis and a very energetic destruction of the pneumococci by the phagocytes take place, while, on the other hand, in fatal infections caused by virulent pneumococci the number of phagocytes in the blood diminishes, and phagocytosis is not apparent. Further work has convinced the author that the crisis is not due to bactericidal properties which have been developed in the body, as he has been able to obtain, even after the crisis, living and virulent pneumococci by puncture of the diseased lung. He has also been able to show that the blood of patients suffering with pneumonia during or even after the crisis does not possess bactericidal properties for the pneumococci procured from the same patient. Rejecting the findings of Isaëff, that the blood of a recovering pneumonia patient possesses active antitoxic properties, the author considers that phagocytosis is the principal factor in the process of recovery. He considers the crisis to be produced by the destruction in the lungs of the majority of the pneumococci by phagocytes. The phagocytosis assumes a more active character in these cases, he thinks, by the appearance in the blood of the stimulins. The

agglutinins, antitoxins, and the other substances of defence are considered to play only a secondary part and to aid in the defence of the organism against pneumococcic infections.

**Histological Studies of Xanthoma.**—Various theories have been advanced in regard to the nature of xanthoma. The tumor has been considered to be derived from atypical and irregular multiplication of sebaceous cells analogous to the carcinoma development of other glands. It has been considered to result from changes in muscle fibres, and has also been thought to be of endothelial origin. The histologic study of xanthoma by McFARLAND and McCONNELL (*Journal of Medical Research*, July, 1904, vol. xii., p. 69) has led them to believe the tumor to be of connective-tissue origin. They found the chief changes in the reticular layer of the cutis, which consisted of an invasion of its tissue by cells penetrating in an irregular manner, resembling the invasion of the alveolar tissue by carcinoma cells. These cells resemble exactly those of the sebaceous glands, and contain a large number of fat-droplets in their cytoplasm. The authors believe these xanthoma cells, as they have been called, to be formed by a very gradual conversion of connective tissue similar to the normal transformation of ordinary connective tissue into adipose tissue.

**Amœbæ: Their Cultivation and Etiological Significance.**—MUSGRAVE and CLEGG (*Report from Bureau of Government Laboratories, Biological Laboratory*, No. 18, 1904) in an interesting article described their method of cultivating amœbæ and the results of a series of animal experiments. A stock medium is prepared in the following manner: agar, 20.000; sodium chloride, 0.300 to 0.500; extract of beef, 0.300 to 0.500.

This is made of 1 per cent. alkaline to phenolphthalein. The medium is prepared in the same way as ordinary sugar, then poured into Petri dishes, and upon the surface is inoculated the material containing amœbæ. So far the amœbæ have only grown in the presence of bacteria. No pure cultures were ever obtained; and in order to procure successful cultivations the importance of this bacterial symbiosis must be taken into account. Usually, in cases of amœbic dysentery, or of "amœbiasis," as the authors have termed this disease, growths of at least one type of bacteria present in the intestines aid the multiplication of the amœbæ. The organisms show a decided selectiveness, however, and when transferred to a plate smeared with a mixed culture of bacteria may pick out a single type. Different growths of amœbæ select different bacteria. Thus, by the use of twelve different selected bacteria, growth was obtained in 30 per cent. of one series of cases, when the control inoculations made on the same medium without bacteria showed only 2 per cent. of positive results. Amœbæ multiply rapidly in from twenty-four to forty-eight hours at room temperature, moving over the surface of the plate. Separate amœbæ could be transferred from one plate to another, so that a single species could be cultivated and studied. In cultures the parasites about the margin of the growth are most actively motile, and frequently multiplication by fission is observed. In older cultures encysted forms are common.

The wide distribution of amœbæ has always been recognized, and the authors have succeeded in cultivating them, not only from the

excreta, intestinal lesions, and liver abscesses in man, but also from 100 samples of water taken from the hydrants in different parts of Manila, from the washings of vegetables, from a number of fruits and various organic matter. In general, it may be said that the whole surface flora of the Philippine Islands carries a large number of these parasites.

Regarding the significance of the presence of these parasites in the intestinal tract, the authors are inclined to believe, though this fact is not yet proven, that all amœbæ are pathogenic or may become so. Further, that they may produce typical lesions in the intestinal tract of man. By feeding cultures of amœbæ from the stools of individuals suffering from dysentery to monkeys, and in one instance to a human being, diarrhœa was produced, fatal to monkeys. In the intestinal discharges the parasites were found, and in monkeys ulcers were seen in the colon. A very important point from a sanitary view was the fact that the disease could be produced by feeding monkeys with cultures of amœbæ obtained from water or from the washings of vegetables.

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**Vaccinia and its Parasite (*Plasmodium Vaccinæ*).—Bosc** (*Centralb. f. Bakt. u. Parasitenkund.*, Orig., 1904, Bd. xxxvii. pp. 39 and 195), from an extensive study of the skin lesions of vaccinia, concludes that this affection is a true inflammatory disease of neoplastic type ("bryocytose") showing rapid evolution and accompanied by the production of immunity toward the sixth day. The disease is due to the development, at first localized, later generalized, of a true parasite, intracellular and belonging to the class of protozoa, the plasmodium vaccinæ.

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**The Differentiation of *Bacillus Diphtheriæ*, *Bacillus Xerosis*, and *Bacillus Pseudodiphtheriæ* by Fermentation Tests in the Serum-water Media of Hiss.**—KNAPP (*Journal of Medical Research*, 1904, vol. xii. p. 475) from a study of 27 cultures of diphtheria bacilli, 10 cultures of xerosis bacilli, and 4 cultures of pseudodiphtheria bacilli concludes that these organisms may be differentiated rapidly and with great ease, according to their behavior upon certain of the sugars. The xerosis bacillus ferments saccharose, while the true diphtheria bacillus does not. Dextrine, on the other hand, is fermented by diphtheria bacillus, but not by the xerosis bacillus. The pseudodiphtheria bacillus differs from both the true diphtheria bacillus and bacillus xerosis, in that it does not ferment any of the sugars tested. Dextrose, mannite, and maltose are all fermented by both the diphtheria bacilli and xerosis bacilli, so that these sugars do not serve to separate the two organisms.

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THE ACTION OF ELECTRICALLY CHARGED COPPER  
UPON CERTAIN ORGANISMS IN WATER.

BY MARY ENGLE PENNINGTON, PH.D.,  
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THAT metallic copper, when placed in water containing algæ or certain bacteria, will kill these organisms seems to be beyond doubt. That the area of copper surface exposed must be quite extensive and that the period of contact is of considerable duration is shown, also, in the experiments already published by a number of investigators. The formation of colloidal copper is, under natural conditions, slow, hence the tardiness in germicidal activity. Could this production of colloidal metal be hastened it is quite possible that a marked reduction in the lethal time would ensue. For the preparation of such solutions the electric current has been found most satisfactory, hence a trial has been made of the action of charged copper plates on certain pathogenic organisms suspended in river water.

As a preliminary experiment, copper foil was placed in a measured quantity of water for twenty-four hours, after which it was removed and weighed. The loss in weight for the same sample of foil was quite constant, being about 0.0006 gram for six square inches of copper surface in twenty-four hours. These copper strips when serving as anode and cathode, with a current of 4 volts and less than 0.01 ampere, lost copper at the rate of 0.0039 gram in one hour. This determination was made a number of times with closely agreeing results.

Other samples of copper-foil gave, under similar conditions, results agreeing among themselves but differing from those already

cited. One sample of copper was, therefore, used throughout this work.

Having determined the rate of removal of the copper from the electrodes, they were placed in water containing *B. typhosus*. In another experiment *B. coli* was used. The water was from the laboratory tap, and was sterilized in an autoclave. Seeding was from an aqueous suspension of the organisms grown on agar slants for eighteen to twenty-four hours at incubator temperature. Control experiments made with water and organisms alone showed practically no change at the end of the experiment period. To determine the action of the current without the copper, platinum strips were substituted, with the result shown in Table 1, C.

TABLE I.—Electrode surface 6 square inches. Current 4 volts, and less than 0.01 ampere. Volume 1000 c.c., 1 c.c. plated.

A.				
	Before treating.	15 minutes, copper 1 to a million.	30 minutes, copper 2 to a million.	45 minutes, copper 3 to a million.
<i>B. typhosus</i>	40,000	115	60	1
	44,000	230	20	1
	107,520	80,500	60	1
	100,400	76,420	36	0

B.				
	Before treating.	15 minutes, copper 1 to a million.	30 minutes, copper 2 to a million.	45 minutes, copper 3 to a million.
<i>B. coli communis</i>	Innumerable.	Innumerable.	89,000	55,600
			180,000	54,500

C.				
	Before treating.	15 minutes, platinum electrodes.	30 minutes, platinum electrodes.	45 minutes, platinum electrodes.
<i>B. typhosus</i>	34,000	24,800	16,200	8,640
	30,000	21,600	18,900	

Is it possible to pass water at the intake of a reservoir over charged copper plates at such a rate that pathogenic organisms, particularly *B. typhosus*, are destroyed in transit? If not killed in transit, would the copper taken up by the water be sufficient to kill them within a reasonable time?

The following very primitive device was used to simulate a reservoir with intake and outlet.

A glass jar of four litres' capacity was fitted with two perforated copper disks, forming the positive and negative poles and exposing about 31 square inches of surface. A wooden cover, carrying inlet and outlet tubes as well as the wires for the electric supply, fitted the top of the jar accurately. Its joint was packed with cotton-

wool as were also the openings for wires and tubes. The entire piece of apparatus, except the copper disks, was sterilized in an autoclave. The copper was sterilized by igniting several times in alcohol, thereby preserving its brightness. A supply jar at a higher level carried an infected stream of water to the bottom of the reservoir whence it flowed up, over and through the perforated disks, and out by a siphon tube, dipping just below the surface of the liquid. Screw clips regulated the rate of flow, and every care was taken to guard against contamination. The amount of copper lost was found by weighing the disks, and was 0.00032 gram per minute. After five minutes' action, then, a litre of water contained 1.6 part copper per million. Plates were made immediately upon the exit of the effluent, and again after it had stood at room temperature for one hour. Controls in water, alone, showed practically no change at the end of thirty minutes nor after one hour.

TABLE II.

	Before treating.	1 minute.	2 minutes.	5 minutes.
B. typhosus	102,600	1360	1380	729
	98,600	1870	1300	900
	180,000	1700	... ..	1000
	170,000	1800	.....	1080

	Before treating.	1 min.	2 min.	5 min.	10 min.
B. coli communis	42,120	3300	2400	980	485
	42,660	4116	2520	1060	600
	43,200	.....	2400	1392	864
	45,900	....	2320	1104	605

After standing for one hour plating the effluent showed the number of organisms per cubic centimetre to be as follows:

Time.	B. typhosus.	B. coli communis.
1 minute . . . . .	36	22
2 minutes . . . . .	7	2
5 " . . . . .	0	0
10 " . . . . .	0	0

A comparison of the foregoing experiments would seem to indicate a balance in favor of a large copper surface with which the organisms come in contact, rather than the actual copper content of the water. Accordingly, another apparatus was arranged in which the water passed over four plates, placed about an inch and a half apart in a glass tube holding 200 c.c.

The copper disks, perforated as before, gave a surface of 9.6 square inches. As the disks were four in number the organisms in their descent were compelled to pass over the four separate surfaces, an interval elapsing between leaving one and reaching the next. Electrolyzed in tap-water, they showed a loss of 0.00014 gram copper per minute for 4 volts and 0.02 ampere. Portions of

500 c.c. were used, giving the water a copper content of 1.4 parts per million for five minutes and 2.8 parts for ten minutes.

TABLE III.

	Before treating.	5 minutes.	10 minutes.
B. typhosus . . .	53,440	sterile.	sterile.
	50,200	"	"
	22,140	1	"
	28,900	3	"

In the making of these experiments the water in which the copper had been electrolyzed was subjected to the ferrocyanide test, and it was noted that when the organisms were not added to the water the reaction was much more distinct than that given by the same quantity of copper in the presence of the bacteria. In the latter case it was sometimes impossible to obtain any reaction with ferrocyanide.

SUMMARY. 1. Copper electrodes carrying a small current are actively germicidal for *B. typhosus* and *B. coli communis*.

2. *B. typhosus* is the more easily affected.

3. That it is the copper which plays the important role is shown by substituting for it platinum electrodes.

I am greatly indebted to Prof. Edgar F. Smith, of the John Harrison Laboratory of Chemistry, University of Pennsylvania, for placing at my disposal the facilities of the electrochemical laboratory, wherein the electric part of this work was carried out.

## STUDIES ON THE BACTERICIDAL ACTION OF COPPER ON ORGANISMS IN WATER.

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THE investigations of Moore and Kellerman<sup>1</sup> on the employment of copper for the destruction of algæ, and incidentally of bacteria, in water, have developed an excellent method for the destruction of certain algæ which have caused a great deal of annoyance, the presence of these cryptogams in water frequently causing a disagreeable odor and taste rendering it unfit for household, and, in many instances, industrial purposes. Such waters while they are not, in the present state of our knowledge on the subject, looked upon as being especially detrimental to the health of a community, will be condemned, and justly, on account of their disagreeable

<sup>1</sup> Bulletin, No. 64, Bureau of Plant Industry.

odor and taste: The same community, however, will use bacteriologically impure water, a much more dangerous water, without considering the question of impurity. The latter, being in many cases clear, odorless, and tasteless, does not appeal to the senses as do those containing algæ, and in spite of all that has been said and done, it is exceedingly difficult to prevail upon many of the populace to take measures which will remove a contamination that is not manifest, *i. e.*, cannot be detected by appearances, and therefore to them does not exist. Should these waters become turbid or show other evidences of pollution they are ready for any measure that will remove the objectionable features. Manifestly, the work of the above-mentioned investigators has been of great value from both a sanitary and an æsthetic standpoint. Furthermore it has caused a great deal of discussion and controversy over one of the most vital questions confronting the sanitarian—namely, that of the destruction of bacteria in contaminated waters. They have shown conclusively, both by laboratory experiments and the practical application of the method, that the repeated treatment of small bodies of water (lakes, ponds, reservoirs, etc.), at comparatively long intervals with small amounts of cupric sulphate will keep them free from objectionable algæ. When we approach the question of destroying bacteria in water by such methods certain factors must be taken into consideration, *viz.*—the contamination usually being continuous, or at frequent and irregular periods, the bactericidal substance must be used continuously and, for various reasons, in as small quantities as possible; therefore the question must be considered from the following standpoints:

(1) Are bacteria destroyed by very dilute solutions of copper salts or by copper in any form?

(2) Which of the copper salts is the most active, and at the same time cheap enough to prevent the question of expense being so great a factor as to exclude its use?

(3) What influence would organic and inorganic substances, from various sources, have on the action of the copper?

(4) Would the constant ingestion of small quantities of copper have a detrimental effect on the health of an individual using water so treated?

While the latter question will not be discussed in this paper we wish to state, for the benefit of the laity and many of the profession who entertain erroneous ideas regarding the subject, that it is not the object of sanitarians, who advocate the use of copper for the purification of water, to use it to the exclusion of other approved methods, such, for instance, as filtration, but to employ it to supplement such methods when the filters are for any reason inadequate; when they are in process of construction; or when filters cannot be immediately installed. And we sincerely hope that work along this line will not convey the idea to anyone that filtration is unnecessary. Also, that



the writer, who when the question was first taken up was strongly prejudiced against the employment of copper for this purpose, has been unable to find any authentic records of chronic poisoning.

The investigation reported in this communication was undertaken to determine to what extent various bacteria are destroyed by dilute solutions of copper salts; and also to show which of these salts has the greatest bactericidal action. Incidentally a few experiments were made with colloidal copper.

The experiments include the action of these substances on *B. typhosus*, *B. coli communis*, *B. dysenteriae*, *B. cloacae*, *B. proteus vulgaris*, *B. prodigiosus*, and the *staphylococcus pyogenes aureus*.

These organisms were selected for the following reasons: Some are pathogenic bacteria causing diseases which frequently follow the use of contaminated waters, and are those which we especially desire to destroy; others while non-pathogenic are frequently, one might say constantly, found in such waters; and the various organisms, possessing different degrees of resistance to the action of bactericidal substances, give us a fair indication of the action of the substances on the majority of non-spore-forming bacteria.

**METHODS OF PROCEDURE.** Flasks containing the various solutions were inoculated with either a small amount of a twenty-four-hour bouillon culture, or a large loopful of bacteria scraped from the surface of a twenty-four-hour agar culture; the organisms were thoroughly distributed throughout the solution and agar plates made immediately, to serve as controls, and one-half and one hour after inoculation, then at intervals of one hour for twelve hours, and if all bacteria were not destroyed within the twelve-hour limit, again at twenty-four hours. The plates were examined at the end of twenty-four hours, and, taking into consideration the facts that some of the organisms employed developed more slowly than others, and that while some might not be destroyed yet their functions would be so inhibited that they would develop slowly, they were counted at the end of forty-eight and again at seventy-two hours, which we consider would be ample time for the development of all bacteria. At least five experiments were made with each organism in the various solutions and dilutions.

**EXPERIMENTS ON THE ACTION OF CUPRIC SALTS.** In these experiments the sulphate, chloride, acetate and nitrate were employed in solutions of 1 : 250,000, 1 : 500,000, 1 : 1,000,000, 1 : 1,500,000, 1 : 2,000,000, made with both distilled and tap-water.

Experiments show the bactericidal properties of the sulphate to be greater than that of the other salts; a solution of 1 : 250,000, as a rule, destroying the *bacillus typhosus* and *bacillus coli communis* in less than one hour; in solutions of 1 : 500,000 and 1 : 1,000,000 they were usually destroyed in two to three hours, while in solutions of 1 : 2,000,000 there was rarely more than 80 to 90 per cent. destroyed in ten hours, and frequently a few would be capable of developing

after twenty-four hours' exposure. Some strains of *B. coli communis* appear to be slightly more resistant than *B. typhosus*. The resistance of *B. dysenteriae*, *B. cloacæ*, *B. proteus vulgaris*, and *staphylococcus aureus* is greater than that of the *B. typhosus* and *B. coli communis*. A solution of 1: 250,000 would not destroy the *B. prodigiosus* in less than five to six hours, and a 1: 500,000 solution would frequently require ten hours for the destruction of this organism. If, however, the bacteria were washed in distilled water before inoculation of the flasks, the resistance was found to have been lessened, due in all probability to the fact that some of the slimy substance which surrounds the bacterial cell and protects it, to some extent, from the action of detrimental agencies, is removed.

The other cupric salts were found to be less active than the sulphate in the following order: chloride, acetate, nitrate.

The following table will serve to show the difference in the action of the various salts on the *B. typhosus* and *B. coli communis*, and of the cupric sulphate on the various bacteria:

COLLOIDAL SOLUTIONS. These experiments were made in both distilled and tap-water as follows:

(1) Inoculation of 100 c.c. flasks of water containing pieces of copper-foil of various sizes.

(2) Inoculation of copper vessels of 500 c.c. capacities.

In the first series of experiments pieces of polished copper-foil giving an exposed surface of from 0.5 to 3 c.c. were placed in an Erlenmeyer flask containing 100 c.c. of water. Some were inoculated immediately, others containing pieces exposing a surface of 0.5 c.m. were placed aside and allowed to stand for ten days before inoculation. In those inoculated immediately after the copper had been placed in the flasks, there was always a reduction in the number of bacteria, but in no instance over 50 per cent. in eight hours, while those in which the foil remained for ten days before inoculation gave results as follows:

*Bacillus typhosus*, 90 per cent. destroyed in two hours, 98 per cent. in three hours, and all in four hours; *bacillus coli*, 50 per cent. destroyed in two hours, 85 per cent. in three hours, 90 per cent. in four hours, and all in five hours; *bacillus dysenteriae*, 83 per cent. destroyed in two hours, 98 per cent. in three hours; in four hours but twenty-five bacteria developed, and all were destroyed in five hours; *bacillus cloacæ*, 20 per cent. were destroyed in two hours, all were not killed until they had been exposed to the action of the solution for ten hours; *bacillus proteus vulgaris*, 97 per cent. destroyed in twenty-four hours; *staphylococcus pyogenes aureus*, 66 per cent. in two hours, at the end of four hours twenty-five colonies developed; in five hours all had been destroyed. The *bacillus prodigiosus* was more resistant, being decreased but 50 per cent. in twenty-four hours.

TABLE SHOWING ACTION OF THE VARIOUS CUPRIC SALTS ON THE  
B. TYPHOSUS AND B. COLI COMMUNIS

Organism.	Salt.	Dilution.	Average number to c.c. in control.	Per cent. destroyed in hours.													
				1	2	3	4	5	6	7	8	9	10	11	12	24	
B. typhosus	Sulphate.	1 : 250,000	110,000														
		1 : 500,000	100,000	99	100												
		1 : 1,000,000	140,000	78													
		1 : 1,500,000	120,000	50	85	99	100										
		1 : 2,000,000	130,000	4	7	55	80	82	87	87	93	98	100				
	Chloride	1 : 250,000	100,000	99	100												
		1 : 500,000	92,000	98	100												
		1 : 1,000,000	95,000	10	20	32	50	62	75	83	92	92	93	94	94	98	
		1 : 1,500,000	103,000	8	14	20	23	40	59	62	64	64	65	65	66	85	
		1 : 2,000,000	114,000	5	10	14	16	21	29	33	34	34	34	35	35	42	
	Acetate.	1 : 250,000	122,000	80	95	99	100										
		1 : 500,000	113,000	66	66	68	70	73	80	89	94	96	100				
		1 : 1,000,000	117,500	7	19	22	30	33	42	42	45	46	46	48	62	95	
		1 : 1,500,000	121,000	5	10	19	23	28	35	36	40	41	55	49	50	75	
		1 : 2,000,000	108,000	2	2	4	9	11	15	22	30	33	33	34	34	65	
	Nitrate.	1 : 250,000	85,000	21	33	40	50	58	71	80	90	93	98	99	100		
		1 : 500,000	82,000	11	20	33	61	60	70	78	84	84	85	85	87	99	
		1 : 1,000,000	91,000	5	10	10	10	11	12	30	32	33	35	37	42	90	
		1 : 1,500,000	98,000	0	3	9	12	14	18	20	20	23	26	37	29	80	
		1 : 2,000,000	79,000	0	0	5	8	12	13	22	22	22	24	25	25	71	
Sulphate.	1 : 250,000	105,000	100														
	1 : 500,000	120,000	99	100													
	1 : 1,000,000	99,000	80	99	100												
	1 : 1,500,000	150,000	87	95	99	100											
	1 : 2,000,000	110,000	8	10	14	27	50	85	90	92	93	93	95	98			
Chloride.	1 : 200,000	160,000	89	99	100												
	1 : 500,000	140,000	58	68	95	97	99	99	99+	100							
	1 : 1,000,000	100,000	20	24	31	38	50	54	65	65	66	67	75	80	98		
	1 : 1,500,000	124,000	10	10	13	15	21	29	32	34	35	38	44	55	89		
	1 : 2,000,000	120,000	2	5	7	13	17	19	23	23	26	29	33	35	73		
Acetate.	1 : 250,000	120,000	78	95	99	100											
	1 : 500,000	130,000	22	38	54	77	81	87	89	96	98	99	99	100			
	1 : 1,000,000	136,600	5	8	11	15	22	36	38	48	57	52	55	62	90		
	1 : 1,500,000	120,000	3	10	10	11	13	16	22	37	...	...	...	...	76		
	1 : 2,000,000	124,000	0	2	6	8	9	11	11	15	18	23	26	28	68		
Nitrate.	1 : 250,000	100,000	13	22	30	30	35	45	51	60	71	75	85	94	100		
	1 : 500,000	100,000	5	10	12	20	20	25	30	35	41	49	58	72	99		
	1 : 1,000,000	104,000	7	10	10	11	12	15	20	30	32	40	51	60	90		
	1 : 1,500,000	91,000	0	2	5	7	8	11	15	25	31	31	34	38	68		
	1 : 2,000,000	92,000	0	0	3	5	5	7	9	12	15	19	25	30	61		

When copper vessels of 500 c.c. capacity, which gave a surface of 266 square centimetres exposed to the water, were employed the action was more marked, the *B. typhosus* and *B. coli communis* being, as a rule, completely destroyed within three hours. The *B. dysenteriae*, *B. cloacae*, and *staphylococcus aureus* and *B. proteus vulgaris* are more resistant. The *B. prodigiosus* always showed a marked reduction in numbers, but was rarely completely destroyed in twenty-four hours. It is interesting to note that two cultures of *B. prodigiosus*, from different sources, employed, while being but slightly decreased in numbers in two to three hours, had almost complete inhibition of their pigment producing function, after exposure to the copper for this period, regaining it, however, after cultivation

for two or three generations on suitable media. The copper must be kept highly polished, as after it has become tarnished the bactericidal action is markedly inhibited.

Flasks containing one litre of a 1:500,000 solution of cupric sulphate were inoculated with relatively large quantities of bacteria, plated and reinoculated at intervals of from two to six hours.

TABLE SHOWING THE ACTION OF CUPRIC SULPHATE ON VARIOUS BACTERIA.

Organism.	Dilution.	Aver'ge No. per c.c. in control.	Per cent. destroyed in hours.												
			1	2	3	4	5	6	7	8	9	10	11	12	24
<i>B. typhosus</i>	1: 250,000	110,000	100												
	1: 500,000	100,000	99	100											
	1: 1,000,000	140,000	78	100											
	1: 1,500,000	120,000	50	85	99	100									
	1: 2,000,000	130,000	4	7	55	80	82	87	87	93	98	100			
<i>B. coli communis</i>	1: 250,000	105,000	100												
	1: 500,000	120,000	99	100											
	1: 1,000,000	99,000	80	99	100										
	1: 1,500,000	150,000	87	95	99	100									
	1: 2,000,000	110,000	8	10	14	27	50	85	90	92	93	93	95	98	100
<i>B. dysenteriae</i>	1: 250,000	11,500	95	100											
	1: 500,000	120,000	40	95	97	100									
	1: 1,000,000	72,000	31	50	62	85	99	99+	100						
	1: 1,500,000	12,400	20	30	40	42	60	70	75	81	85	87	90	91	100
	1: 2,000,000	13,600	20	20	25	30	30	45	60	62	62	68	71	75	98
<i>B. cloacae</i>	1: 250,000	92,000	90	99	100										
	1: 500,000	86,000	68	90	99	100									
	1: 1,000,000	101,000	33	85	89	96	96	99	100						
	1: 1,500,000	89,000	5	10	30	40	70	85	95	98	98	99	100		
	1: 2,000,000	94,500	3	10	31	40	80	83	85	88	91	91	93	97	100
<i>B. proteus vulgaris</i>	1: 250,000	115,000	93	100											
	1: 500,000	106,000	65	92	98	100									
	1: 1,000,000	111,000	28	51	82	90	95	98	100						
	1: 1,500,000	99,000	10	18	27	42	69	90	93	98	99+	100			
	1: 2,000,000	118,000	0	12	22	36	51	65	78	80	85	88	92	95	100
<i>B. prodigiosus</i>	1: 250,000	102,000	95	99	99	99+	100								
	1: 500,000	109,900	15	26	80	95	97	99	99+	100					
	1: 1,000,000	110,000	9	11	16	33	33	45	47	61	63	69	...	...	93
	1: 1,500,000	107,000	4	12	17	30	38	46	46	48	51	52	60	61	92
	1: 2,000,000	98,000	0	1	8	8	10	11	15	30	38	41	43	50	88
<i>Staphylococcus pyogenes aureus</i>	1: 250,000	92,000	99	100											
	1: 500,000	88,000	50	70	90	100									
	1: 1,000,000	86,000	15	30	30	70	78	85	97	99	99	100			
	1: 1,500,000	100,000	8	22	28	96	58	69	85	93	95	99	100		
	1: 2,000,000	95,000	1	8	10	30	50	64	79	82	85	98	99	99+	100

The results show that after a series of inoculations the bactericidal action of the solution gradually decreases.

The action was greater when distilled water was used for making the dilution than when tap-water was employed. Very little difference was found between the distilled and the filtered water used in the laboratory. The bacteria from agar cultures were more readily destroyed than those in bouillon cultures; this might be explained by the fact that a small amount of bouillon, 0.05 to 0.1 c.c., was added to the solution with the bacteria.

The question arises: Why is the bactericidal action of the sulphate greater than that of the other copper salts? Many of the metallic salts precipitate albuminous substances—*e.g.*, those of mercury and copper; in fact, salts of most of the heavy metals. These by coagulating the protoplasm will kill the organism. In the precipitation there is formed a compound of the metal with the albumin. One would naturally consider that the compound containing the highest percentage of the metallic element would possess the greatest bactericidal activity. Such, however, is not the case, and we are compelled to look farther for an explanation. Krönig and Paul,<sup>1</sup> in an investigation on the action of various chemicals on bacteria, showed that certain compounds varied, in their action, in proportion to the degree of electrolytic dissociation. Copper sulphate undergoes dissociation into its positive and negative ions more readily than the other cupric salts. The copper ion combines with certain constituents of the bacterial cell, either destroying it directly or rendering the cell wall impermeable so that nutritive substances cannot be absorbed. Colloidal copper in all probability acts in the same manner.

The results obtained seem to warrant the following conclusions:

(1) Dilute solutions of copper salts have a marked destructive action on many bacteria. Of these salts the sulphate is most active. This is probably due to the fact that it undergoes electrolytic dissociation more readily than the others.

(2) The amount of sulphate to be used in the water should be from one part in 250,000 to one part in 100,000, depending on the character of the water.

(3) Colloidal copper will quickly destroy certain bacteria; should copper vessels or plates be used to destroy bacteria in water they must be kept highly polished or the bactericidal properties will be greatly reduced.

(4) We have been unable to find evidence of copper, ingested in small quantities for long periods, having a detrimental action on the health of an individual.

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## A STUDY OF THE ACTION OF COLLOIDAL SOLUTIONS OF COPPER UPON *BACILLUS TYPHOSUS*.

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THE excellent work done some months ago by the Bureau of Plant Industry, Department of Agriculture, in Washington, on the destruction of algæ and certain pathogenic bacteria by the solution

<sup>1</sup> Zeitschrift f. Hygiene, 1897, Bd. xxv.

of salts of copper and the colloidal solution of copper led us to undertake this work along similar lines.

The small numbers of algæ in the waters of the Schuylkill and the Delaware Rivers have not, up to the present time, caused any special contamination of the reservoirs or the filters of the Philadelphia water supply.

The suspected contamination, however, of our river water with typhoid and the numerous epidemics of typhoid fever in this community make every method or means brought forward to diminish the death-list from typhoid fever worthy of the greatest attention and of most careful investigation.

By colloidal solution of copper is meant the solution of metallic copper that takes place when a bright copper surface is brought into contact with water. -

Different grades of copper do not all give off the same amount of colloidal copper, and on account of the different bacterial content, and because of the varying amount of vegetable and mineral matter in solution, typhoid bacilli and water organisms are not always acted upon in exactly the same time or in the same way by colloidal copper solutions.

The waters of the Delaware and the Schuylkill rivers show a great variation in number of bacteria per cubic centimetre in different seasons. This variation is from 200 germs per cubic centimetre to many millions.

For comparison and control, this experimental work was not carried on in test-tubes, as was done in previous experiments, but in copper and other metallic vessels of different sizes varying from one-fourth litre to eight litres in capacity.

The following experiments given in detail were made to determine, if possible, the action of metallic copper upon typhoid organisms and upon the ordinary river-water organisms of both the Schuylkill and Delaware Rivers.

The action of metals—tin and aluminium—and of glass upon the same organisms was determined under the same circumstances as the action of copper.

The vessels used in these tests were made with a lid for filling, and a small opening in the lid closed with a plug of cotton for the convenient testing of the contents.

### *Experiment to Determine the Life of Typhoid Organisms in Copper, Tin, and Glass Vessels.*

Copper, tin, and glass vessels of various sizes were filled with tap-water (Schuylkill), and sterilized in an autoclave at 18 pounds' pressure for thirty minutes.

These vessels were inoculated with 1 c.c. per litre of suspension of typhoid organisms in water and thoroughly shaken.

Plates were made in one hour, three hours, and in twenty-four hours.

The water in the glass vessels was exposed freely to the light; this, no doubt, had a marked influence upon the destruction of the organisms.

The experiment was conducted at room temperature.

The suspension of typhoid germs used was made in sterile water, and contained 270,000,000 organisms per cubic centimetre. One cubic centimetre of this suspension was used to each litre of water.

Character and size of the vessels.	No. of sq. inch surfaces exposed.	Count within 1 hour.	Count in 3 hours.	Count in 24 hours.
8 litre copper . . . .	287	4,400	0	0
8 litre tin . . . .	287	32,480	29,973	3,650
8 litre glass . . . .	330	12,300	14	0
4 litre copper . . . .	193	9,900	0	0
4 litre tin . . . .	193	25,280	44,500	6,700
4 litre glass . . . .	184.5	24,680	3,280	200
2 litre copper . . . .	124	5,460	0	0
2 litre tin . . . .	124	24,910	28,960	8,400
2 litre glass . . . .	130	8,400	18	0
1 litre copper . . . .	79	4,053	0	0
1 litre tin . . . .	79	52,930	40,760	9,660
1 litre glass . . . .	80	14,130	10	10
$\frac{1}{2}$ litre copper . . . .	48	6,646	0	0
$\frac{1}{2}$ litre tin . . . .	48	20,000	48,000	141,200
$\frac{1}{2}$ litre glass . . . .	52	45,000	15,400	640
$\frac{1}{4}$ litre copper . . . .	25	1,960	0	0
$\frac{1}{4}$ litre tin . . . .	25	25,600	68,130	7,800
$\frac{1}{4}$ litre glass . . . .	28	14,260	148,000	176,850

In this experiment the typhoid organisms were all killed within three hours in the copper vessels.

In the glass vessels there was considerable variation due, possibly, to the differences in glass, and the tin vessels showed also a great variation in their effect.

#### *Experiment to Determine the Life of Typhoid Organisms in Filtered Water in Copper Vessels.*

In this experiment 250 c.c. of filtered water, showing an absence of germs, was placed in a sterile copper vessel of 250 c.c. capacity and an exposed surface of 25 square inches, and was inoculated with 1 c.c. of a suspension of typhoid organisms which contained 150,000,000 germs per cubic centimetre.

The germs were thoroughly mixed in the water, and plates were made in fifteen minutes, one hour, two hours, three hours and twelve hours.

Time of count.	Colonies per c.c.
15 minutes . . . .	30,000
1 hour . . . .	3,800
2 hours . . . .	1,200
3 " . . . .	0
12 " . . . .	0

*Experiment to Determine the Life of Typhoid Organisms in Water Sterilized in a Glass Vessel in an Autoclave and Transferred to a Copper Vessel which had been Sterilized by Direct Flame and then Inoculated.*

500 c.c. of water was sterilized in a glass vessel in an autoclave under 15 pounds' pressure for one-half hour and was, after cooling, poured into a sterile copper vessel, having an exposed inner surface of 48 square inches and inoculated with 2 c.c. of a suspension of typhoid in water containing 150,000,000 germs per cubic centimetre.

Counts were made in fifteen minutes, one hour, two hours, three hours, and twelve hours.

Time of count.	Colonies per c.c.
15 minutes . . . . .	43,000
1 hour . . . . .	1,570
2 hours . . . . .	1,400
3 " . . . . .	0
12 " . . . . .	0

*Experiment to Determine the Life of Typhoid Organisms in Sterile Tap-water in a Copper Vessel which had been Cleansed with Lemon-juice and Salt, and Rinsed with Hot Water.*

In this instance 2 c.c. of a watery suspension of typhoid bacilli containing 12,000,000 germs per cubic centimetre were added to a two-litre copper vessel filled with sterile tap-water and left at room temperature.

Counts were made immediately in one hour, two hours, three hours and twelve hours.

Time of count.	Colonies per c.c.
15 minutes . . . . .	43,860
1 hour . . . . .	78
2 hours . . . . .	11 (?)
3 " . . . . .	0
12 " . . . . .	0

*Experiment to Determine the Life of Typhoid Organisms in Raw Tap-water in a Copper Vessel.*

A four-litre copper vessel having an exposed surface of 193 square inches was cleansed thoroughly with lemon-juice and salt, and then washed in hot water.

The vessel was filled with tap-water having 1030 organisms per cubic centimetre and was inoculated with 4 c.c. of a watery suspension of typhoid organisms which contained 12,000,000 germs per cubic centimetre, and allowed to stand at room temperature.

The counts were made immediately, in one hour, two hours, three hours, and twelve hours.

Time of count.	Colonies per c.c.
Immediately . . . . .	15,090
1 hour . . . . .	15,000
2 hours . . . . .	15,200 few typhoid.
3 " . . . . .	13,800 no "
12 " . . . . .	0



The rapidly growing water organisms obscured the typhoid organisms so quickly that the counts were difficult to make, and the experiment was repeated.

This experiment was repeated in a two-litre copper vessel filled with ordinary tap-water having 150 water organisms per cubic centimetre.

The exposed copper surface was 124 square inches.

The water was inoculated with 2 c.c. of watery suspension of typhoid organisms containing 3,360,000,000 germs per cubic centimetre and allowed to stand at room temperature (75°), and counts were made every fifteen minutes for three and a half hours.

Time of count.	Typhoid germs, per c.c.	Water germs, per c.c.
Immediately . . . . .	18,000	150
$\frac{1}{4}$ hour . . . . .	12,000	110
$\frac{1}{2}$ " . . . . .	7,800	110
$\frac{3}{4}$ " . . . . .	4,200	120
1 " . . . . .	2,400	125
$1\frac{1}{4}$ hours . . . . .	2,160	112
$1\frac{1}{2}$ " . . . . .	1,440	115
$1\frac{3}{4}$ " . . . . .	340	103
2 " . . . . .	360	100
$2\frac{1}{4}$ " . . . . .	120	104
$2\frac{1}{2}$ " . . . . .	24	95
$2\frac{3}{4}$ " . . . . .	0	90
3 " . . . . .	0	92
$3\frac{1}{4}$ " . . . . .	0	60
$3\frac{1}{2}$ " . . . . .	0	60

*Experiment to Determine the Life of Typhoid Organisms in Sterile Tap-water Contained in a Copper Vessel.*

A 500 c.c. copper vessel having an exposed surface of 48 square inches was cleansed with lemon-juice and salt, and washed with hot water and filled with sterile tap-water.

The water was inoculated with 1,081,000,000 typhoid organisms.

Counts were made immediately and every fifteen minutes for three and a half hours.

Time of count.	Typhoid germs, per c.c.	Water germs, per c.c.
Immediately . . . . .	18,000	0
$\frac{1}{4}$ hour . . . . .	1,280	0
$\frac{1}{2}$ " . . . . .	82	0
$\frac{3}{4}$ " . . . . .	68	0
1 " . . . . .	0	0
$1\frac{1}{4}$ hours . . . . .	0	0
$1\frac{1}{2}$ " . . . . .	0	0
$1\frac{3}{4}$ " . . . . .	0	0
2 " . . . . .	0	0
$2\frac{1}{4}$ " . . . . .	0	0
$2\frac{1}{2}$ " . . . . .	0	0
$2\frac{3}{4}$ " . . . . .	0	0
3 " . . . . .	0	0
$3\frac{1}{4}$ " . . . . .	0	0
$3\frac{1}{2}$ " . . . . .	0	0

*Experiment to Determine the Amount of Colloidal Copper in Solution.*

A one-litre copper vessel was filled with tap-water and allowed to stand for three hours at room temperature (75°).

The surface of copper exposed to the action of water was 79 square inches.

A test was made by Dr. Robinson to find the amount of colloidal copper in solution.

He reported that there was one part of copper to 4,000,000 parts of water, or one square inch gave off one part to 316,000,000 parts of water.

In many of the experiments much less time than three hours was required to kill off all the typhoid organisms.

The action of infinitesimal amounts of copper is remarkable.

*Experiment to Determine the Resistance of Typhoid Organisms and Schuylkill River Organisms to Colloidal Solutions of Copper.*

One litre of Schuylkill water taken at Market Street was placed in a clean copper vessel.

A bacterial count made immediately showed approximately 400,000 germs per cubic centimetre.

Another litre of water from the same source was placed in a sterile glass beaker and kept in the dark.

A count of the bacteria in this water also showed approximately 400,000 organisms per cubic centimetre, counts of the water bacteria in the glass beaker every fifteen minutes for six hours were as follows:

Time of count.	No. of colonies.	Time of count.	No. of colonies.
$\frac{1}{4}$ hour . . . .	400,000	$3\frac{3}{4}$ hours . . . .	550,000
$\frac{1}{2}$ " . . . .	454,000	$3\frac{1}{2}$ " . . . .	530,000
$\frac{3}{4}$ " . . . .	475,000	$3\frac{1}{4}$ " . . . .	550,000
1 " . . . .	450,000	4 " . . . .	595,000
$1\frac{1}{4}$ hours . . . .	450,000	$4\frac{1}{4}$ " . . . .	560,000
$1\frac{1}{2}$ " . . . .	460,000	$4\frac{1}{2}$ " . . . .	550,000
$1\frac{3}{4}$ " . . . .	450,000	$4\frac{3}{4}$ " . . . .	560,000
2 " . . . .	475,000	5 " . . . .	580,000
$2\frac{1}{4}$ " . . . .	480,000	$5\frac{1}{4}$ " . . . .	560,000
$2\frac{1}{2}$ " . . . .	480,000	$5\frac{1}{2}$ " . . . .	560,000
$2\frac{3}{4}$ " . . . .	480,000	$5\frac{3}{4}$ " . . . .	560,000
3 " . . . .	500,000	6 " . . . .	600,000

To the copper vessel filled with Schuylkill water was added 3 c.c. of a suspension of typhoid organism containing about 2,888,000,000 germs per cubic centimetre.

Counts were made every fifteen minutes for six hours.

In one and three-fourth hours no typhoid organisms could be found in the water, that would grow on plates.

After three hours the water in the copper vessel was poured into a glass vessel and allowed to remain there, protected from the light.

One set of plates was allowed to remain at room temperature and another duplicate set was kept in an incubator at (37° C.).

In six hours the number of organisms remained stationary.

Time of count.	No. organisms per c.c. agar plates grown in incubator.	No. organisms per c.c. agar plates grown in room temp..75°.
At once		
¼ hour	960,000	960,000
½ "	950,000	920,000
¾ "	925,000	923,000
1 "	605,000	600,000
1¼ hours	525,000	350,000
1½ "	350,000	168,000
1¾ "	250,000 no typhoid.	120,000 no typhoid.
2 "	237,000 "	115,000 "
2¼ "	237,000 "	115,000 "
2½ "	212,000 "	120,000 "
2¾ "	187,000 "	95,000 "
3 "	180,000 "	95,000 "
3¼ "	175,000 "	95,000 "
3½ "	168,000 "	90,000 "
3¾ "	150,000 "	75,000 "
4 "	120,000 "	50,000 "
4¼ "	105,000 "	52,000 "
4½ "	95,000 "	50,000 "
4¾ "	95,000 "	53,000 "
5 "	95,000 "	50,000 "
5¼ "	93,000 "	47,000 "
5½ "	90,000 "	52,000 "
5¾ "	90,000 "	53,000 "
6 "	90,000 "	50,000 "

*Experiment to Determine the Effect of Colloidal Copper upon Delaware River Water Germs and upon Bacillus Typhosus.*

500 c.c. of Delaware River water collected at Market Street wharf was placed in a copper vessel containing 48 square inches of inside exposed surface, and a similar quantity was placed in a glass vessel, and light excluded from both vessels.

The experiment was conducted at room temperature (75°).

The water when placed in the vessels contained 384,000 germs per cubic centimetre.

DELAWARE RIVER WATER.

Time of count.	Organisms per c.c.
Immediately	384,000
In glass, three hours	240,000
In copper, three hours	18,000

To the water in the copper vessel was then added 3 c.c. of a suspension of typhoid bacilli containing 396,000,000 germs.

Counts were made at intervals of fifteen minutes of the contents of both the copper and the glass vessels.

At the expiration of two hours the typhoid bacilli had entirely disappeared from the water in the copper vessel and the water organisms had been reduced to 5400 per cubic centimetre; while in the glass vessel 150,000 water organisms per cubic centimetre were present.

Time of count.	Copperish water containing 18,000 river-water organisms plus 396,000,000 typhoid germs.	Plain Delaware water containing the 240,000 river organisms per c.c.
At once . . . . .	288,000	240,000
15 minutes . . . . .	163,300	230,000
30 " . . . . .	57,600	220,000
45 " . . . . .	30,000	200,000
1 hour . . . . .	13,300	200,000
1¼ hours . . . . .	10,000	180,000
1½ " . . . . .	8,000	200,000
1¾ " . . . . .	7,500 (no typhoid noted).	150,000
2 " . . . . .	5,400	150,000

*Experiment to Determine the Life of Typhoid Bacilli in Water that has been kept in a Copper Vessel in Comparison with that which has been kept in a Glass Vessel.*

Water sterilized in an autoclave in a glass vessel was used in this experiment.

A litre of this water was placed in a copper vessel having an inside surface of 79 square inches and another litre of water was placed in a glass vessel and light was carefully excluded.

Both vessels were allowed to stand for three hours at room temperature.

At the end of that period the water in the copper vessel was poured into a glass vessel similar to the control and light excluded.

4 c.c. of a suspension in water of bacillus typhii containing about 10,000,000,000 were placed in each vessel and counts were made at intervals of fifteen minutes for two hours.

The three hours' exposure of the litre of water to the 79 square inches of copper surface was, as previously stated, dissolved, 1 part of colloidal copper to 4,000,000 parts of water.

Time counts were made	No copper present. No. of colonies per c.c.	Copper present 1 part to 4,000,000. No. of colonies per c.c.
At once . . . . .	7,630,000	3,600,000
15 minutes . . . . .	7,296,000	2,760,000
30 " . . . . .	7,800,000	2,400,000
45 " . . . . .	7,600,000	1,680,000
1 hour . . . . .	6,100,000	540,000
1¼ hours . . . . .	4,840,000	480,000
1½ " . . . . .	4,800,000	180,000
1¾ " . . . . .	3,040,000	17,000
2 " . . . . .	2,920,000	0 (16)

The influence of the colloidal copper present is shown most conclusively by this experiment.

*Experiment to Determine the Length of time Required for Typhoid Organisms to Die in Copper Vessels, Aluminium Vessels, and Enamel Ware Vessels.*

Vessels of the same general shape and size were cleansed with hot water, and 1000 c.c. of sterile water placed in each.

To each vessel was then added 16,875,000 typhoid organisms, and counts were made every half hour.

Time count was made	Copper. Colonies per c.c.	Aluminium. Colonies per c.c.	Enamel. Colonies per c.c.
Immediately . . .	42,800	43,200	42,500
½ hour . . .	6,480	43,000	45,000
1 " . . .	36 (?)	10,800	27,000
1½ hours . . .	0	5,400	27,000
2 " . . .	0	3,800	27,000
2½ " . . .	0	960	21,000
3 " . . .	0	0	20,000

CONCLUSIONS. (1) There is a natural tendency for typhoid bacilli to die when the water containing them is allowed to stand for a long period. There may be a temporary increase in the number, but this is followed in several hours or days by a decrease and a final disappearance.

(2) Trials were made as to the period of total disappearance of typhoid organisms which had been placed in sterile Schuylkill water and in that taken directly from the tap, and from the river surface containing large numbers of water organisms. These waters were placed in vessels of glass, porcelain, tin, and copper and their contents kept at room temperature were plated every fifteen minutes for periods ranging from three to six hours. All the experiments were repeated many times.

(3) Sterile drinking water in clean copper vessels inoculated with typhoid bacilli invariably showed that the bacilli had all perished in one hour. Water similarly treated in tin vessels invariably showed living organisms at the end of twenty-four hours. Water similarly treated in glass vessels exposed to light showed varying results, but in no instance had the typhoid organisms all perished in three hours. Water similarly treated in enamel vessels showed a slight diminution of the number of typhoid organisms in three hours. Water similarly treated in aluminium vessels showed a disappearance of the typhoid organisms in three hours.

(4) Raw tap-water in glass vessels showed an increase in the number of organisms in three hours; occasionally, there was a slight diminution in their number. Raw tap-water in copper vessels in one experiment showed a diminution from 384,000 germs per cubic centimetre to 18,000 per cubic centimetre in three hours. Usually the diminution was not so great. Raw tap-water containing large numbers of river organisms and considerable vegetable

matter, when inoculated with millions of typhoid organisms and placed in a copper vessel, showed that the typhoid were killed off in one and three-fourths hours to two and one-half hours.

(5) Water containing colloidal copper has a more rapid tonic action upon typhoid organisms than upon river-water organisms.

(6) The quantity of colloidal copper given off from a one-litre copper vessel in three hours was one part to four million. This amount killed off the added typhoid organisms in from one and three-fourths to two and one-half hours, and chemical experience has shown that this amount of colloidal copper is harmless when taken into the human system.

(7) In epidemics of typhoid fever water could be purified of typhoid organisms by allowing it to stand in a copper vessel for three hours.

## GLIOMA OF THE NOSE.

### REPORT OF TWO CONGENITAL CASES.

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"The glioma is a tumor consisting of proliferated neuroglia (the supporting tissue of the central nervous system) and of bloodvessels which are accompanied by a small amount of connective tissue." Mallory says further, in the article from which the above quotation is taken, that it is found exclusively in the central nervous system of which it forms the commonest tumor, that it is essentially a benign growth, does not give rise to metastases, but is dangerous partly on account of the pressure it exerts, partly from destruction of the nervous tissue it infiltrates. On account of its vascularity, large and small hemorrhages are not infrequent. Mallory also says: "Gliomata of the retina have not been discussed in this article because no one has yet shown by modern differential stains that they occur." In this connection the following quotation from Ohlmacher is pertinent: "Most of the so-called gliomata originating in the retina, especially in children, are in reality a form of round-cell sarcoma with pronounced metastatic tendencies, which glioma lacks." Other writers, as Senn and Bland-Sutton, speak as if the existence of glioma of the retina in childhood were established. Senn mentions glioma as having been found in the acoustic nerve, and, as a heterotopic tumor, in the kidney, the ovary, and the testicle.

There seems to be some difference of opinion, therefore, among writers on this subject, as to whether or not true glioma ever occurs

outside the brain or spinal cord. But no writer denies that the appearance of this growth anywhere except in the regions just mentioned is very rare. In view of these facts, the two following cases would seem to be worth recording as of unusual importance and interest.

CASE I.—Edward K., aged two years, of American parentage, was brought to the throat clinic of the Massachusetts General Hospital in April, 1903, on account of a rounded tumor of the nose, about the size of a robin's egg, which his mother said he had had from birth and which caused considerable deformity, as the photograph shows. The tumor was soft to the touch and resembled very strongly in appearance and consistency a fatty tumor. There was no pulsation in the swelling nor any change in its consistency when the child cried, so that, although its site and general appearance suggested a possible meningocele, it was assumed as reasonably certain that, at the time the child was seen, the tumor had no direct connection with the brain cavity. On looking into the nose, the left nostril was observed to be almost completely obstructed by a pinkish-gray, polypoid growth, the origin of which could not be definitely determined, although its connection with the external tumor could hardly be questioned. A piece of the growth was removed from the left nostril by means of cutting forceps. Hemorrhage was free but ceased quickly. This specimen was submitted to Dr. J. H. Wright, director of the clinico-pathological laboratory of the hospital, who made the following report:

"Microscopic examination of the specimen sent for examination shows that it consists of a piece of tissue partly covered with mucous membrane. The tissue making up the greater part of the specimen consists chiefly of delicate fibrils and peculiar cells and is clearly atypical neuroglia, as shown by its histological appearance and by the staining reaction of the fibrils. This neuroglia tissue near the mucous membrane gives place to submucous connective tissue, but is not sharply marked off from this connective tissue. In fact, it is seen infiltrating the spaces of this tissue after the manner of a sarcoma.

"Diagnosis. As far as the specimen itself goes, the condition is to be regarded as glioma. The glioma may be in continuity with the brain, but it seems to the pathologist more likely that it is associated with a teratomatous tumor in the neighborhood.

"J. H. WRIGHT."

In view of the unusual character of the growth and the uncertainty of the prognosis it was decided to keep the child under observation for a time before undertaking to remove the tumor, if that were eventually thought advisable. The photograph was taken and the mother was told to bring the child again at a stated time. But she never returned, and no answer could be obtained to several letters.

As the case was a much too important one to be entirely lost sight of, the writer finally made a trip to the city where the patient lived, about twenty-five miles from Boston, and after some difficulty

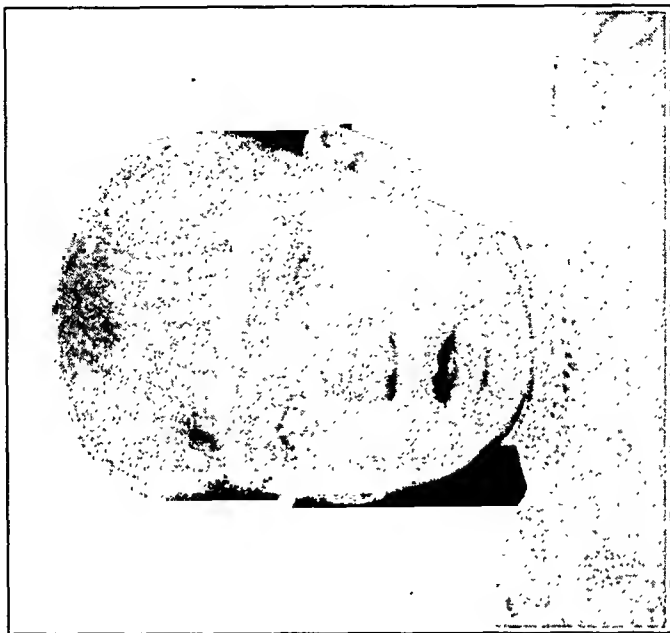
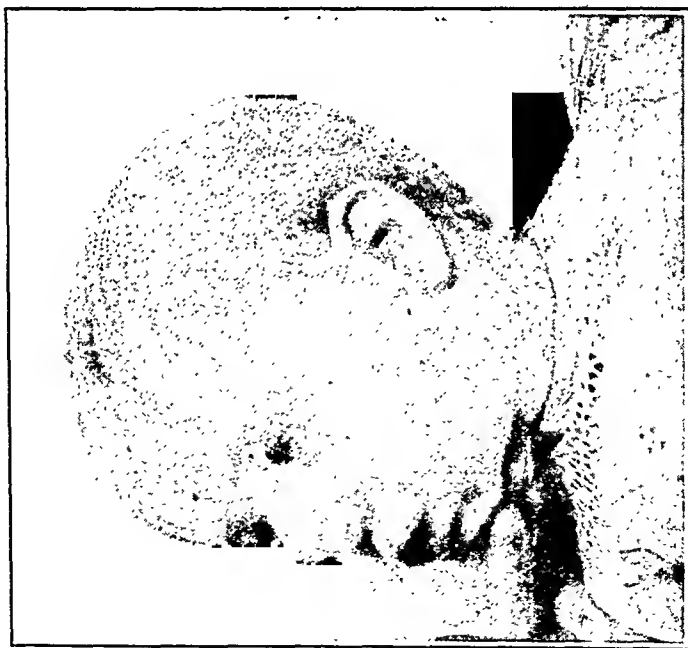


FIG. 1.



Photographs of Case I.

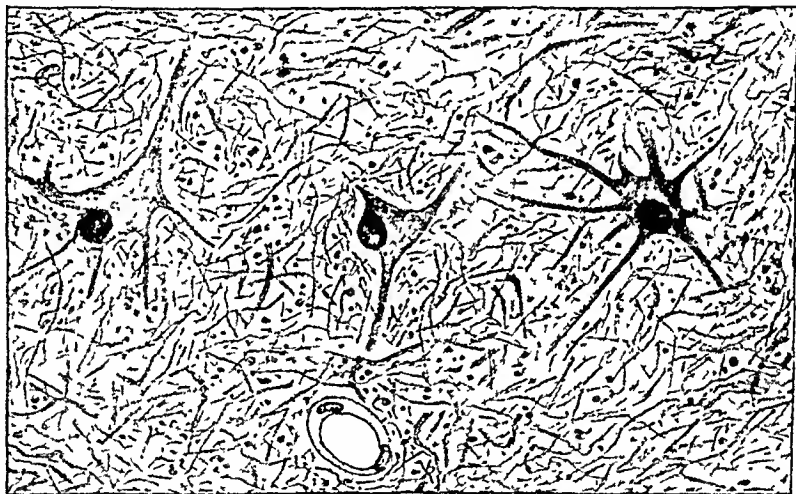
owing to the family having moved, found the boy. It was learned that he had been operated on at a local hospital on June 23, 1904. The tumor had evidently been removed, as the nose was normal



except for a rather unusual breadth and a rather prominent linear nearly vertical scar, about 2 cm. in length. The general health of the child appeared excellent, and there was no local evidence of any new-growth. Communication with the hospital where the tumor had been removed elicited the facts that it had not been preserved and that no microscopic examination had been made of it. Nor could any description of the gross appearances at the operation be obtained. Interesting as these reports would have been in completing the history of this case, the diagnosis is sufficiently established by Dr. Wright's report.

The second case was first seen at the throat clinic of the Massachusetts General Hospital on December 21, 1903, by Dr. Frederic C. Cobb, who was then on duty, and he very kindly referred it to me.

FIG. 2.



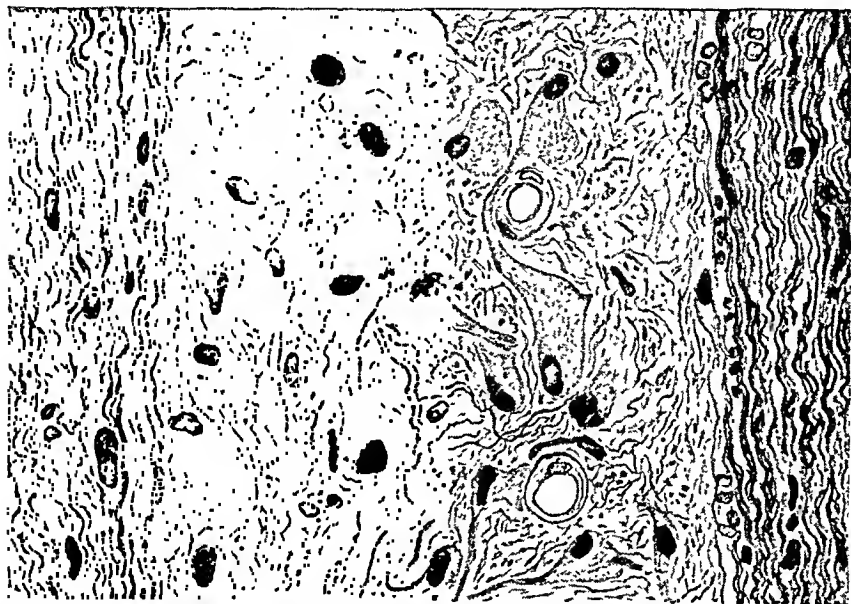
CASE I.—High-power drawing from a paraffin section of the material removed by operation, showing the character of the tumor tissue, which is composed of fibrils and "spider" glia cells.

CASE II.—William A. M., aged ten weeks, was brought to the hospital on December 21, 1903. The father said that the child had not breathed well through the nose since birth and that he had noticed something in the left nostril. The infant appeared in excellent health and took its nourishment well except for the inconvenience caused by partial nasal obstruction. On examination a pinkish-gray polypoid mass was seen in the left vestibule, causing almost complete obstruction of that side. The site of the growth was higher up in the nose, and, as nearly as could be discovered, owing to the difficulty of seeing into so small a nostril, appeared to be the septum. A piece was snared off for microscopic examination. Hemorrhage was free but easily stopped by slight pressure. The pathologist's report on this specimen and on another removed in February, 1904, was as follows:

"On December 21, 1903, and on February 29, 1904, small pieces of tissue were excised from the lesion on the nasal septum. Microscopic examination of both these specimens shows, in the situation of the submucosa of the part, masses of a peculiar tissue which has the structure and staining reaction of a gliomatous tissue. The tissue consists of cells and fibrils in varying proportions. Some of the cells are quite large, have eccentric nuclei and fibrillary processes. This gliomatous tissue in places appears to infiltrate and distend lymph spaces, and columns of it may be seen in the submucosa very near the mucous membrane proper.

"J. H. WRIGHT."

FIG. 3.



CASE II.—High-power drawing from a paraffin section of the material obtained by operation, showing part of a column of gliomatous tissue infiltrating the submucous connective tissue. The tissue, composed of the paler fibrils and the large pyriform cells occupying the middle portion of the drawing, is the gliomatous tissue. The darker fibrils on each side of the drawing represent the connective tissue of the submucosa.

Another specimen was removed on April 20th, and was reported to be practically the same as the first. No photograph of this patient was taken because there was no external deformity. At the date of writing this paper, December, 1904, this child is in excellent health and there is no apparent increase in the growth.

These are certainly genuine cases of glioma outside the central nervous system. They resemble each other closely in every particular except that in one there was an external deformity. They were both evidently of prenatal origin. It is unfortunate that no record of the operation in Case I. could be obtained, for it might have cast some light on the source of the tumor. The writer is inclined to the opinion that these growths arose, during the process of fetal development, through the shutting out of some neuroglia

or, more exactly, that embryonic tissue which becomes neuroglia from the brain cavity in the coming together of the two lateral halves of the frontal bone. In both cases, as far as the histories go, the tumor appears to be absolutely benign. In the first case the tumor had not changed in size from birth up to two years of age, according to the mother's observation. It was removed six months ago, nearly, and there is no sign of recurrence. It is about a year since the other case was first seen. During this time the growth has shown no apparent increase. The writer will endeavor to keep in touch with these cases, and if there are any new developments he will report them. A thorough search of medical literature for a period of more than ten years past reveals no other reported case of glioma of the nose.

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## A CASE OF CEREBROSPINAL RHINORRHOEA, WITH RETINAL CHANGES.

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AND

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A REPORT of this case is important as a contribution to the collected cases of a very rare affection and likewise as an additional evidence of the importance of the eye-ground changes in obscure conditions affecting the central nervous system. In 1899 Dr. St. Clair Thomson published an elaborate and altogether admirable monograph which contains the fruits of a painstaking search through medical literature for instances of a curious affection of which the most conspicuous symptom is the spontaneous escape from the nose of cerebrospinal fluid. He succeeded in unearthing the clinical records of 20 cases in which a watery flow from the nostril could with reasonable certainty be regarded as originating from the cranial cavity. Many cases in which the predominance of evidence spoke for other possible sources of the watery flow—*e. g.*,—nasal hydrorrhoea, dropsy of the antrum, serous accumulation in the maxillary sinus, vasomotor neuritis, and ruptured lymph tubes—were carefully differentiated and excluded.

These 20 cases, then, or 21 including the case investigated by Thomson, may properly be regarded as instances of this curious affection. In commenting upon his monograph the *British Medical Journal* has this to say, and in no better way than by quoting from its editorial can the debt which medicine owes to Dr. Thomson for his careful study of this little-understood disease be expressed: "From the dust-heaps of medical literature he has been able to unearth the details of no fewer than 8 undoubted cases similar to his own and 12 others which were probably of the same character. These cases were, as a rule, described and indexed under different titles. In addition, in the works of Willis and Morgagni, there are records of others which are suggestive of this condition; so that cerebrospinal rhinorrhœa is no new disease, but one which, though undoubtedly rare, may not be so uncommon as would at first be thought."

That the disease is indeed rare can be seen from the few reported cases and also from the fact that, in a personal letter to the authors, St. Clair Thomson states that, though constantly on the lookout for similar cases, his published case remains the only one in his experience. His large clinic at Kings College Hospital and the Throat Hospital has in over five years yielded no additional example of this affection.

At the time of Dr. Thomson's report such a case had an interest that at present does not exist. The escape of cerebrospinal fluid from the nose in quantities sufficient for purposes of examination gave an opportunity for the study of this fluid which up to that time did not often present itself. At the present time it is always an easy matter to obtain a sufficient amount by lumbar puncture for all purposes of laboratory study. It is scarcely to be wondered at that such men as Halliburton, Hill, and others should have made elaborate studies of the fluid from Thomson's case in regard to the chemical, bacteriological, and morphological contents of the collected specimens. Their work has made it possible to determine in a given case whether the fluid so obtained is cerebrospinal or simply a secretion from the nose due to other causes.

A certain number of the cases which have been reported and those contained in the original monograph have been accompanied by optic neuritis and optic atrophy. Of the 20 cases discussed by Dr. Thomson, 8 presented more or less severe affections of the nerve-head and retina adjacent. These 8 cases, which are probably all the cases in literature of cerebrospinal rhinorrhœa with ocular complications up to 1899, together with Freudenthal's and the present case, have been tabulated by us with reference to vision, the state of the pupils, the condition of the fundus oculi, the visual and color fields, the time relation of the ocular symptoms and the nasal flow, the nostril from which the fluid escaped, and miscellaneous ocular symptoms:

Author.	Vision.	Pupils.	Fundus oculi.	Visual fields.	Time relation of ocular symptoms and nasal flow.	Flow from right or left nostril.	Other ocular symptoms.
Leber. Von Graefe's Arch f. Ophthalm., 1883, vol. xxix., Hft 1, p. 273.	O. D. V., fingers. O. S. V., hand motion. 4 yrs. later, O. D. V., 0. O. S. V., fingers.	React promptly.	Right disk blanched, papillary and retinal vessels narrowed. L. disk blanched, nasal border indistinct, smaller veins tortuous.	Greatly contracted except in upper vertical meridian.	Flow 5 years after failure of vision.	Left.	Color blindness.
Mackenzie. Trans. Intercolonial Med. Congress of Australasia, Third Sec., Sydney, 1892, p. 500. Körner. Zeitschr. f. Ophthalmik., July, 1897, Bd. xxiii., Hft 1.	V., p. 1., both.  O. D. V., 5/6. O. S. V., fingers.	Partly dilated, equal, react slightly to light.	Optic neuritis, both; three years later, optic atrophy.	.....	Flow 1 year after failure of vision.	Left.	
Baxter. Brain, January, 1892, vol. iv., p. 523.	O. D. V., 12/60. O. S. V., 12/60. Later vision failed nearly to blindness.	R. normal, good light reaction. L. dilated, no reaction to light; reaction to accommodation present. Equal, react well.	Optic atrophy, both.	.....	Flow several years after failure of vision.	Left.	Slight prominence of globe; rotatory nystagmus; insufficiency of innervation.
Netteship. Ophthalmic Review, 1883, vol. ii., p. 1.	O. D. V., 20/100. O. D. V., 20/70 with —1 sph. C —1.25 cyl. O. S. V., 20/30, not improved.	Large and sluggish.	Postpapillitic atrophy, veins tortuous, vessels shrunken.	Incomplete hemipia, upper and outer quadrant of each visual field defective.	Flow 2 years before failure of vision.	Right.	Color perception normal.
Priestley Smith. Ophthalmic Review, 1883, vol. ii., p. 4.	O. D. V., faint p. 1. O. S. V., 0.	.....	Disks atrophied.	.....	Flow 1 year after failure of vision.	Left.	Color perception normal.
Priestley Smith. Ibid., p. 7.	V. both, 0.	Dilated.	Double optic neuritis, later atrophy.	.....	Flow 4 years after failure of vision.	Left, later right.	Horizontal nystagmus; R. eye making larger excursion than L. Nystagmus.
Emrys-Jones. Ibid., 1888, vol. vii., p. 97.	O. D. V., 9/6. O. S. V., fingers to outer side.	.....	R. Disk pale, atrophic L. well-marked atrophy.	Marked concentric contraction.	Flow 2 years after failure of vision.	Right, later left; right nostril occluded by polyp.	
Freudenthal. Virchow's Archiv, Bd. cxli, Hft 2, p. 323.	O. D. V., 20/30. O. S. V., 20/100.	React well.	R. mild grade of papillitis. L. neuroretinitis.	.....	Flow 10 years before failure of vision. Flow 6 months before failure of vision.	More discharge from left than right. Left.	Color perception normal.
Authors' Case.	O. D. H. 1.25, V. 10/15. O. S. H. 1.25, A. 0.75, Mc. 90, V. 10/24.	Equal 4 mm. diameter; react sharply to light and accommodation.	Partial postpapillitic atrophy, both.	Moderate concentric contraction for white, more marked concentric contraction for blue, red, and green.	Flow 4 years after slight failure of vision.	Right.	Color perception normal.

In all cases the ophthalmoscopic pictures were strikingly similar: either a full-blown optic neuritis passing into atrophy, or typical postpapillitic atrophy. The pupils were usually dilated, reacting feebly to light stimulation. In 5 cases the visual fields were examined and found contracted. The only instance of examination of the color fields was in a case reported by Nettleship, who found the field for green very much contracted, while that for red almost equalled the white field. Central color perception was found normal in 4 cases; color blindness in 1. The severity of the inflammatory process and its destructive effect on the fibres of the optic nerve may be judged from the fact that the visual outcome in 5 cases was bare perception of light or total blindness. In the remainder, one eye, although presenting indubitable ophthalmoscopic evidence of participation in the inflammatory process, still retained a fair measure of vision. In the case reported by Emrys-Jones the better eye attained a vision of 6/6 after correction of its ametropia. Nystagmus was observed in 3 cases. Slight prominence of the globe and insufficiency of the interni were noted in 1 case (Körner).

In 4 cases it will be observed that the greater visual defect obtained in the eye on the same side as the nasal flow. Failure of vision preceded the establishment of the flow in 7 cases, the interval being from one to five years. In 3 cases the flow began several years before the onset of ocular symptoms.

CASE.—Miss Z., servant, aged thirty-two years, was referred to Dr. Schwab by Dr. H. W. Loeb, the laryngologist, for examination of her nervous system. Her chief symptom was a continuous watery discharge from the right nostril in the presence of an absolutely negative nasal and throat condition. Her family history indicates a definite neuropathic stock. One sister died in an insane asylum. Two brothers are living, of whom one shows many of the symptoms of the patient other than the nasal ones. One sister died of tuberculosis. The patient has always been considered of a nervous temperament, and she herself has been aware of this condition. Her history shows several attacks of illness of a vague nature, from which she recovered slowly under a more or less systematic rest. None of these attacks show any trace of an infectious or organic origin. Seven or eight years ago there was a period of a year or more during which she was not able to work for any length of time, yet with no definite symptoms other than fatigue. She was easily tired, had headaches frequently, and was unable to sleep. Rest and a vacation afforded relief. About four years ago she was suddenly attacked by a paralysis of the left leg, which compelled her to remain in bed for some weeks. The leg was not painful, but was stiff and weak. From this she recovered fully, no trace remaining. The present trouble began about two years ago, following a cold, or at any rate the patient first noticed at this time the discharge from the nostril. The fluid dropped continuously

from the nostril day and night. The amount varied from time to time from a few drops to 3 or 4 c.c. in an hour. When the patient is worried or fatigued the flow increases. The fluid is clear, tasteless, and does not stiffen or stain the handkerchief. If the patient reads or inclines the head to the right the amount of the escaping fluid is increased. There is no pain or any discomfort other than the necessity of always taking care of the discharge. Occasional headaches, of which the patient complains, are not in any way influenced by the amount of discharge. Six years ago the patient had an attack of "pink eye," recovering promptly under treatment. In 1899 she noticed some haziness of vision, accompanied by symptoms of asthenopia. The report obtained from the oculist who treated her at that time is as follows: "Neuroretinitis; swelling of 3 D. in the right disk; left disk, beginning atrophy."

The physical examination of the internal organs shows no abnormality. The nervous system gives evidence of a neurasthenic-hysterical group of symptoms, not particularly well marked. The knee-jerks are increased, as are the plantar and Achilles reflexes. The Babinski reflex is not present. The sensory system shows some anomalies. The conjunctiva and the pharyngeal mucosa are anæsthetic. There is a marked hyperæsthetic area in the small of the back, which is very tender to the slightest pressure. The fingers and hand show a very marked tremor, coarse and slow, not affected by rest or motion. The urine is normal with the exception of a rather high specific gravity. As all the specimens examined showed this high specific gravity, it is probable that the continual leakage of fluid from the nostril accounts for it. The patient is distinctly hypochondriacal, much interested in her condition, for which she is convinced a disease of the spinal cord is responsible.

Many specimens of the fluid were examined, collected under different conditions, and in varying amounts from a few drops to several cubic centimetres. There was little difference in the specimens so studied. The fluid is clear, odorless, and tasteless. Specific gravity about 1010. No albumin and no mucin were found. In one specimen there was obtained a reduction by Fehling's test. Centrifugalized specimens showed, beyond a few leukocytes, nothing abnormal and no other formed elements.

*Ocular Examination.* Pupils equal 4 mm. in diameter. Direct light reaction sharp. Consensual a little sluggish. Reaction to accommodation present. Ocular movements unrestricted in all directions. No tendency to outward deviation of either eye during strong convergence. With Maddox rod, esophoria 2°, no hyperphoria. Nystagmus absent. The accommodative power is normal for the age of the patient. The refraction, estimated under homatropine cycloplegia, proved to be: O. D.—H. 1.25 D.; V = 16/15. O. S.—H. 1.25; Ah. 75; Mc. 90; V = 16/24. Color perception normal. No central scotomata.

*Ophthalmoscope.* Right eye: Disk generally pale; outer margin clearly outlined, inner a little blurred. Veins moderately full and slightly tortuous. Arteries distinctly narrowed and "corkscrewly." Grayish stippling of retina around disk. Macula and periphery of fundus normal. Left eye: Disk blanched, the outer quadrant occupied by a glistening white, semicircular area. Veins narrowed; arteries much contracted and "corkscrewly." Extensive grayish stippling of retina surrounding disk. Macula and periphery of fundus normal.

The charts show a moderate concentric contraction of the visual field for white and a more marked concentric contraction of the color fields. It will be noted that the degree of peripheral defect is greater in the left eye, which, visually and ophthalmoscopically, has evidently sustained the brunt of the inflammatory mischief.

The dropping from the nose first observed in April, 1903, has always been from the right nostril. It did not appear, therefore, until four years after the onset of the neuroretinitis. The greater degree of atrophy is found in the nerve on the side opposite the dripping nostril. In both respects the case offers a contrast to the majority of the cases in the table.

The feature in which the present case differs conspicuously from the clinical picture of hitherto recorded cases of cerebrospinal rhinorrhœa consists in the preservation of a high and almost equal degree of visual acuity in both eyes, despite indubitable evidence of inflammatory and atrophic changes in both optic disks. It should be borne in mind, therefore, that while the type of optic neuritis in this disease is usually severe and greatly destructive of sight, a much milder form (Baxter, Nettleship, and the present case), running a typical inflammatory course without seriously impairing the fibres of the nerve, is occasionally encountered. Wholly unimpaired central visual acuity cannot justify the assumption that there is no disease of the optic nerve. A rigorous ocular examination, with especial reference to the visual and color fields, may disclose the presence of optic-nerve mischief in a majority if not in all cases of cerebrospinal rhinorrhœa. This phenomenon should then properly be regarded as an integral part of the symptom complex and not merely as a complication.

Since the publication of Dr. St. Clair Thomson's monograph, only one case of this condition associated with optic neuritis has, so far as we can ascertain, been recorded. Freudenthal describes a case of watery flow from the left nostril in which an optic neuritis developed eight months later. Vision reduced to O. D. 20/30; O. S. 20/100. The ophthalmoscope showed a mild grade of papillitis in the right eye and a frank neuroretinitis in the left.

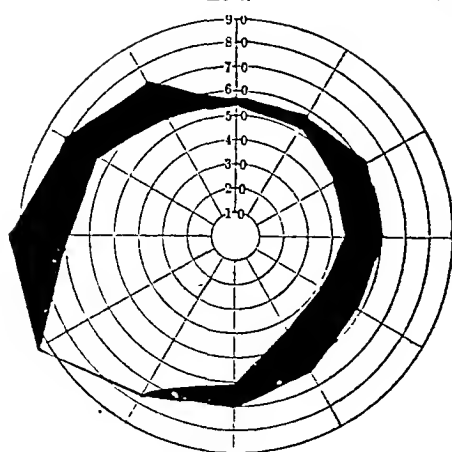
The diagnosis of the case as one which properly belongs to that class of cases which St. Clair Thomson reports cannot be in much doubt. The chief question at issue is the decision in regard to the



CHART I.

White.

Left.



Right.

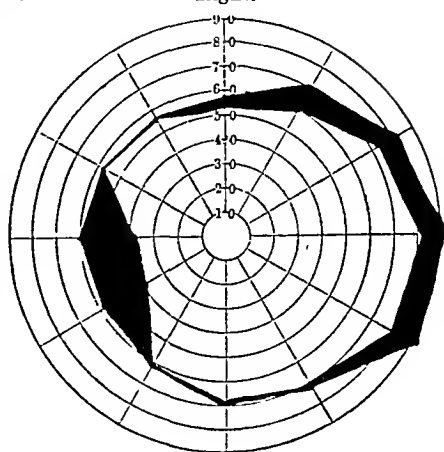
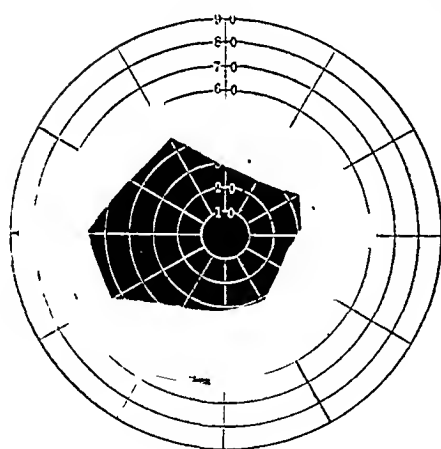


CHART II.

Blue.

Left.



Right.

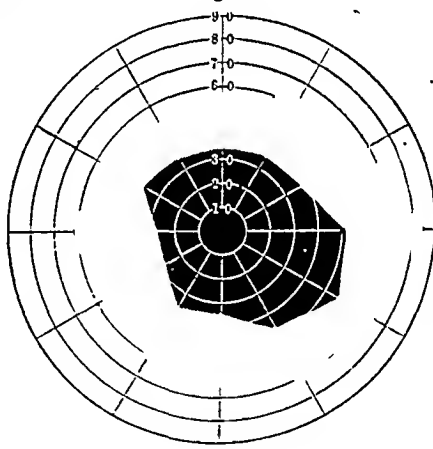
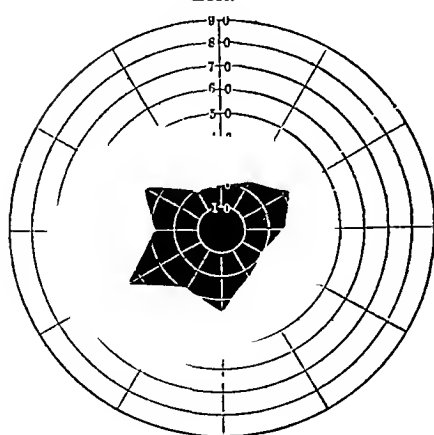


CHART III.

Red.

Left.



Right.

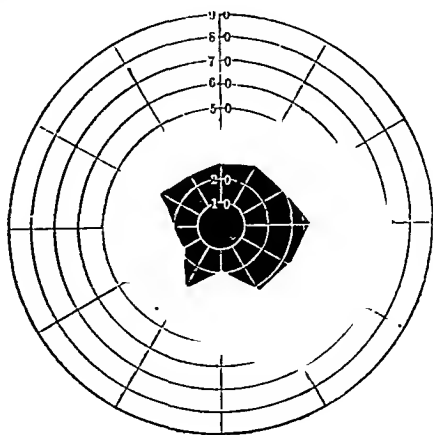
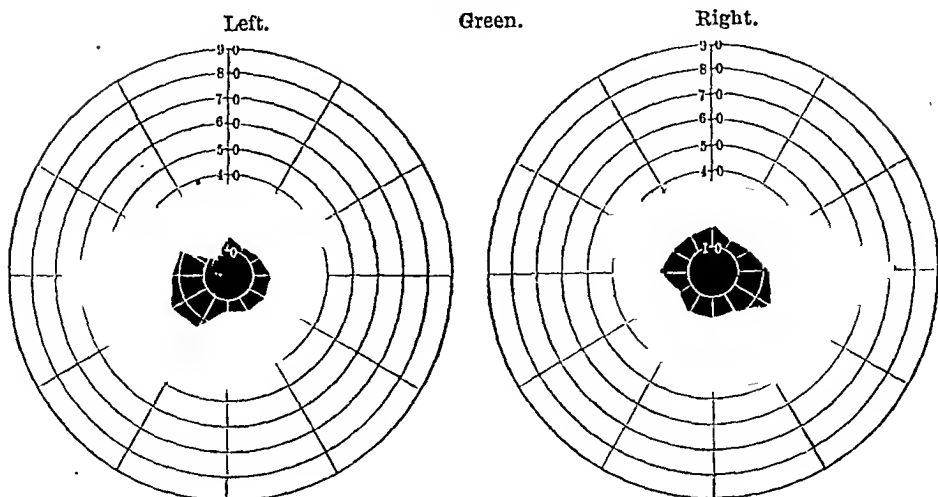


CHART IV.



fluid. If it can be said to be cerebrospinal in character, then the diagnostic problem is solved. That it is possible to determine this with absolute certainty is due to the work of Halliburton and Hill, as was previously pointed out. Halliburton distinctly says that this fluid stands apart from all other similar fluids. "The diagnosis of cerebrospinal fluid from other forms of watery flux from the nose need not in future present any difficulty. The constant and long-continued escape from the nostril of a perfectly clear watery fluid should always arouse a suspicion as to its subarachnoid origin. When this fluid is found to be free from taste, smell, and sediment; when albumin and mucin are found to be practically absent from it, and when Fehling's solution is reduced by it, the suspicion becomes a certainty."<sup>1</sup>

In regard to the etiology of this strange affection we can add nothing of importance. Whether it is due to some inflammatory process or whether it is in part due to certain anatomical defects in the skull are at present open questions. The presence of the ocular changes are, therefore, of great importance because they seem to point to the fact that there must have been some general process of perhaps an inflammatory or circulatory character which first made itself evident in the optic nerve and then afterward gave rise to the other symptom, namely, the release of cerebrospinal fluid from the skull through the nose. The assumption that there is in some of these cases, particularly the one reported by Freudenthal, a cerebral tumor which is the causative agent we believe to be unfounded.

The point which we especially desire to emphasize is that the ocular changes in these cases are probably not accidental, but are an integral part of the disease of which they form one part and the escape of the cerebrospinal fluid forms the other.

<sup>1</sup> British Medical Journal editorial.

A CASE OF MIND BLINDNESS UNIQUE IN THAT THE  
ENTIRE MESIAL SURFACE OF BOTH OCCIPITAL  
LOBES AND BOTH OPTIC RADIATIONS  
WERE PRESERVED.<sup>1</sup>

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ISLAND, W. STATE HOSPITALS FOR THE INSANE.

I DESIRE to place on record the clinical history of a patient with mind blindness, and a report of the gross and microscopic conditions found in his brain. The case is, so far as I can discover, unique; the patient suffered for a long period from a form of blindness, yet no lesion was found on the mesial surfaces of the occipital lobes or in the optic radiations, as is the rule in cases of mind blindness. But symmetrical areas of softening were present in the outer cortex of each cerebral hemisphere, including on each side the angular and supramarginal gyri. I am indebted to Dr. Wilgus for the patient's history while in the King's County Hospital, to Dr. Simon for his history while in the King Park Hospital, to the late Dr. Williams for the autopsy report, and to Dr. C. B. Dunlap, of the New York State Hospitals' laboratory; for excellently prepared sections of the brain, eyes, and optic nerves.

W. S., male, aged fifty-three years, was seen by me at the Long Island State Hospital for the Insane at King's Park, October 19, 1902. His pupils were of medium size and responded promptly to light, and his fundi were normal. He was, however, apparently unable to count fingers and his eyes did not follow a light. Nevertheless he seemed to me to be visually aware of the presence of persons in the room, and although at first glance he impressed one as blind, the ward attendants were sure that at times he saw, and his behavior differed from that of patients in the same ward blind of optic nerve atrophy.

My frequent examinations revealed no changes in the pupils or fundi up to the time of his death, August 26, 1903, ten months later.

At this point I might say that the retinae and optic nerves when examined microscopically were found to be normal.

When I first saw the patient he was demented, aphasic, and extremely obstinate, so that extended psychical examinations could not be carried out, and hence I was largely dependent upon the records of hospitals in which he had been previously and upon the anamnesis furnished by his wife, an intelligent woman.

<sup>1</sup> A preliminary report of this case was read before the American Ophthalmological Society, July, 1904.

The chief points in his history are as follows: Eight years before his death he staggered one day while in the street, and after reaching home was found to be numb on one side and unable to speak intelligibly. The following day he seemed quite well again and returned to his work—that of roasting coffee.

In March, 1902, seventeen months before his death, he came home one night feeling ill. On arising the next day he bumped into objects, apparently being blind. His mind was confused and he was unable to speak intelligibly. He went to bed and remained there a week, after which he was able to get up, but his left arm and leg were very weak. He had become emotional and depressed. He refused to take objects handed to him, or to feed himself, or to help himself in any way. He accused his wife of infidelity and was ugly, refusing to answer her questions.

In June, 1902, with his wife he visited his mother-in-law. At her house improvement was noticed and at times he talked quite rationally with his mother-in-law, whom he liked. Speech was difficult and memory for recent events was very poor. He seemed to see, but he never tried to read. When he walked his wife always led him because of his muscular weakness, and therefore it was difficult for her to judge of his powers of orientation.

At this time he had frequent visual hallucinations, believing, for example, that he saw men in the street when no one was there.

In July, 1902, he failed both physically and mentally, and then ceased to answer questions. On some days he bumped into objects, on others he seemed to see. He talked thickly and besides this failed to recall the words he wished to use. He was fond of smoking, but now when he took his pipe in his hand he was unable to fill it or even to hold it properly, not knowing whether he was grasping the bowl or the stem (apraxia), and he puffed away contentedly when an empty pipe was placed in his mouth, provided that a match had been struck and held near it.

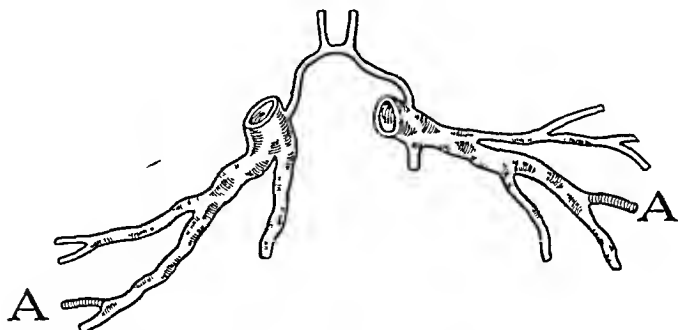
In the King's Park Hospital he slowly wasted away, and died finally of enteritis. His wife frequently visited him, and up to the last she thought that on some days he saw, since he would answer correctly when she asked him if she had on her hat or gloves, or some question of this sort. On other days he refused to answer such questions, and on these days she believed him to be blind.

To sum up, this was a case of dementia after hemiplegia, together with aphasia, apraxia, and an interference with vision which much of the time amounted evidently to total blindness.

There are doubtless several forms of mind blindness. This case was apparently not of the commonest form, which has been much studied in recent years, particularly by Liepmann. In the common form of mind blindness the patient unquestionably sees but does not recognize what he sees. That is, perception takes place probably in the lower cortical visual centre about the calcarine fissure,

but there is destruction or cutting off of the higher centres of visual apperception which lie presumably in and about the angular gyri. With this form of mind blindness there are, as a rule, hemianopic

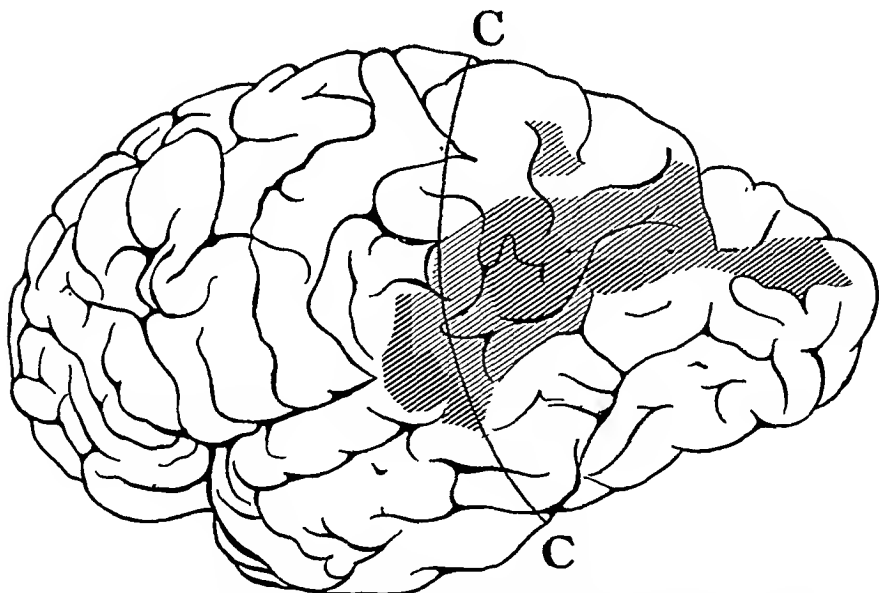
FIG. 1.



The internal carotids and their branches, sclerotic in patches. *A A*, blocked parieto-temporal branches of the middle cerebral arteries.

defects in the visual fields, and frequently aphasia and also astereognosis—the inability to recognize objects by the touch, or apraxia—the inability to handle objects recognized. The patients have arteriosclerosis, and occlusion of cerebral arteries leading to softening in the occipital lobes is the anatomical cause of the

FIG. 2.



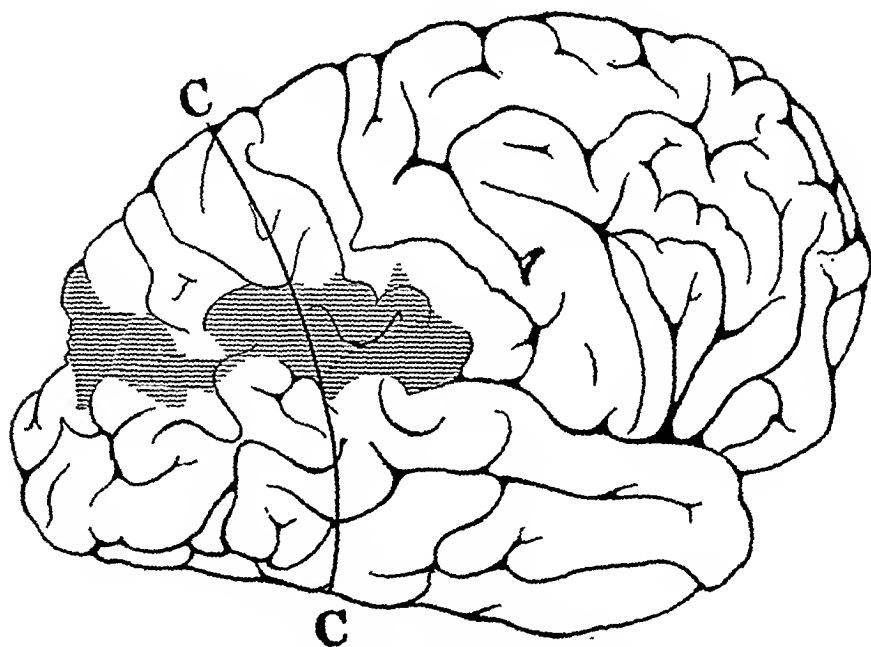
The softened areas in the left hemisphere, indicated by shading, the darker shading indicating the more marked destruction.

mind blindness. In the cases reported, so far as I can learn, there has always been found, besides other lesions, either destruction of the cortex near the calcarine fissure on the mesial surface

of the occipital lobe, or destruction of the optic radiation. Yet there are cases on record in which there was bilateral destruction of the calcarine cortex without true mind blindness; hence it has been supposed that the cortical centres whose destruction or cutting off cause mind blindness lie outside of the cuneus.

In this case the vessels of the brain exhibited many patches of sclerosis and the parieto-temporal branch of each middle cerebral artery, which runs in the fissure of Sylvius, was occluded from the point where it was given off (Fig. 1, *AA*). This occlusion had caused softening in an extensive area in each hemisphere, including the angular and supramarginal gyri, and reaching back on each side nearly to the tip of the occipital lobe (Figs. 2, 3 and 4). There was,

FIG. 3.



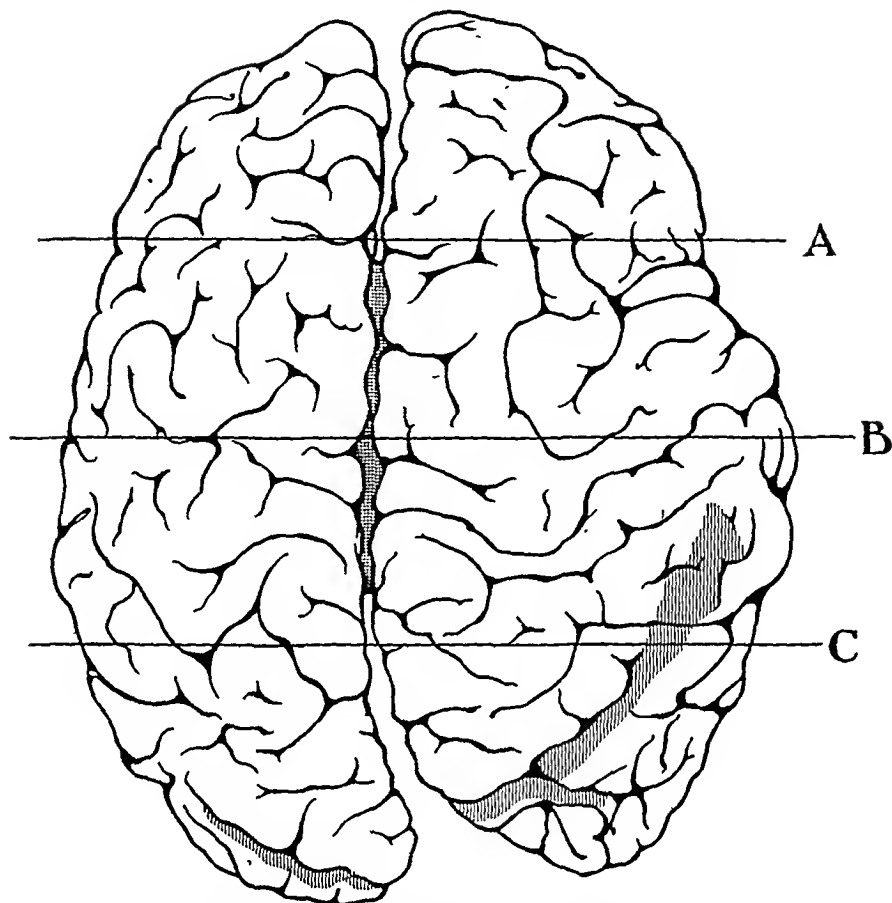
The softened areas in the right hemisphere.

however, no softening on the mesial surface of the occipital lobes, and in a frontal section 4.5 cm. anterior to the tips of the occipital lobes the softening of the outer cortex on each side was found to extend only to the upper margin of the tract of white matter whose lower portion is supposed to contain the optic fibres (Fig. 5, *WW*).

In microscopic sections the softening extended no deeper than is shown in Fig. 5. And in serial sections 1 mm. apart stained by Weigert's method the visual fibres which run from the external geniculate bodies through the optic radiations were not degenerated. In other words, the connection between the external geniculate body and the calcarine cortex on each side was unbroken.

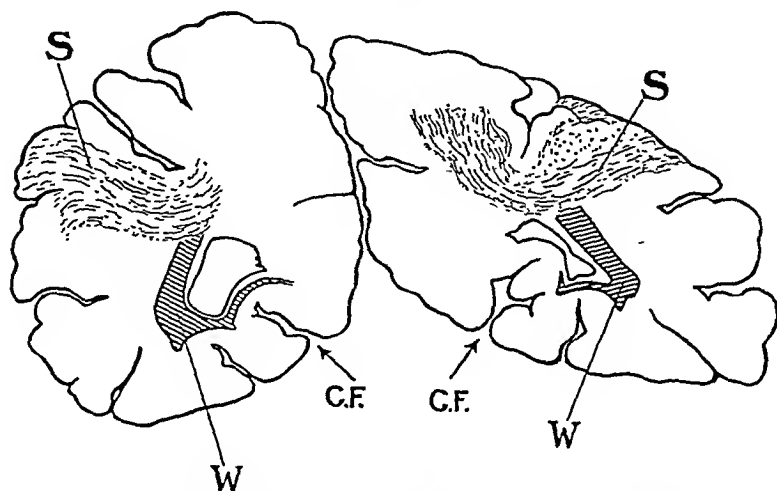
Thus this case differs from the ordinary case in that here calcarine cortex and optic radiations were preserved. Here the primary visual

FIG. 4.



The shading indicates the softening as seen from above. Considerable distortion of the brain took place in the hardening process.

FIG. 5.



The softened areas *SS* as seen from behind in a section of the distorted brain at *CC* (Figs. 2, 3 and 4): *CF*, calcarine fissures; *WW*, the tracts of white matter which include the optic radiations.

pathways from retinae to calcarine fissures were normal. But softening of the angular gyri and the parts adjacent, in which it is believed the higher visual centres lie, produced such marked disturbance of vision that it was a question much of the time whether the patient had any power of visual perception.

This case then shows that extreme disturbance of vision may be brought about by lesions in the higher cortical visual centres alone, to which we ophthalmologists have, as yet, given little attention.

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## PURPURA HEMORRHAGICA.

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THE report of this case is of interest, in addition to the interest aroused by rather rare cases, because of the close resemblance in clinical course of some cases of Werlhof's disease to cases of acute leukæmia which are not infrequently reported in the literature of to-day. This resemblance has not been commented upon by most writers on acute leukæmia, nor by the authors of books upon blood diseases, with the exception of Bézangon and Labbé,<sup>1</sup> who class purpura hemorrhagica among the pseudoleukæmic states.

J. S., aged sixteen years, nativity Ireland, was admitted to the Dispensary of Cornell University Medical College May 3, 1902. His complaint was weakness and inability to work following closely upon severe epistaxis, which occurred without warning and without apparent cause. For two years he had worked in the "filing department" of a neighboring brass foundry. The family history was satisfactory, including no "bleeders," and neither deaths nor sickness suggesting the less common diseases; he was one of six healthy children.

The history of the patient's early years, obtained from his mother, was that of a healthy, active boy who escaped the exanthematous and infectious diseases of infancy and childhood, apparently without a day's illness until two weeks before coming under observation. For one year the boy had smoked cigarettes and a pipe, but not to excess. There was no history and no evidence of venereal disease. Rarely a glass of beer was taken. The usual diet consisted of ham, eggs, potatoes, tea, toasted bread, with fresh meat and other vegetables at least twice a week, and under treatment

<sup>1</sup> *Traité d'hématologie*, 1904, p. 683.



the substitution of fresh meat and vegetables and fruit did not influence the course of the disease.

Twelve days before admission he stopped work on account of increasing weakness, which was first noticed the day following a severe "nose-bleed," fourteen days before admission. During the six days following the initial severe epistaxis slight bleeding continued "by spells" each day, and at this time the pallor was noted and the spitting of blood occurred for the first time. No soreness of the mouth was complained of and the parent and the boy thought the latter bleeding from the lung, although on admission the condition of the gums would have accounted for a moderate amount of "blood spitting." The urine was not noticed during this period of two weeks, and had been previously always "clear and yellow;" but twelve days before admission the stools were noted as black and sticky, and the same description was applied later to the stools, which were found to contain much blood and blood pigment.

At no time were there chills, rigor, headache, nausea, or vomiting to suggest the onset of an acute infection. There were loss of appetite and loss in weight.

*Physical Examination.* Fairly well nourished boy. Facies sickly, pale, a yellowish pallor, ears bloodless; dark-red, crusty particles about nares and corners of mouth. Conjunctivæ pale. The tongue was pale and covered with a black coating, which he stated was from his medicine (iron). The right tonsil was swollen; the left tonsil normal; no swelling of left or right cervical glands. The gums were soft, but only slightly swollen, and from them constantly oozed thin, watery blood. A few small blebs,  $\frac{1}{2}$  mm. in size, were on the right eyelids. Temperature by mouth  $101^{\circ}$ .

*Thorax.* Thin and shallow, symmetrical; expansion fair.

*Lungs* percussed normally, and sounds were normal over right and left fronts and backs.

*Heart.* Maximum impulse in fifth space well inside nipple line; area normal. Over the point of maximum impulse and extending inward and upward toward the pulmonic region was heard a soft, systolic, blowing murmur, greatest intensity at the apex; a similar murmur in the second and third left spaces over the pulmonic area. The pulse was 120 to the minute, small and regular.

*Abdomen.* Soft, not tender; stomach area normal; spleen not palpable and area not enlarged by percussion; liver area normal, edge not palpable in right midclavicular line. No rose spots.

*Hemorrhagic Eruption.* Scattered over the upper thorax, back and front, and the neck were a few small, irregular spots suggesting bruised areas, varying in color from a purple to a yellow color. No petechiæ, and no fresh cutaneous hemorrhages. Over the sacrum was a large (10 x 13 cm. = 4 x 5 inches) purple-red purpuric spot which had appeared twenty-four hours previously, tender on pressure, but no tumor and no induration. Over the external

surfaces of both thighs just above the knees, over the legs just below the knees, and over the lower portion of the legs were scattered numerous, irregular, purpuric spots of a greenish-yellow color, varying in size from 1 to 4 cm. in largest diameter. No history of injury. No œdema about ankles.

*Rectal examination* was negative. No hemorrhoids and no evidence of infection about anus or in lower rectum.

*Genitalia.* Puerile; otherwise normal.

*Glands.* No glandular enlargement.

*Blood Examination,* May 3, 1902. Coagulation time seven to nine minutes (Wright). Hæmoglobin, 33 per cent. (von Fleischl); red blood corpuscles, 1,916,000; white blood corpuscles, 3000.

*Malaria.* Parasites not found.

Red cells fresh and stained appeared normal, excepting moderate polychromatophilia; no erythroblasts. Differential (400 cells): polynuclears, 50.3 per cent.; lymphocytes, 38.3 per cent.; large mononuclears, 11.3 per cent.

*Urine.* Clear; light yellow; 1012; albumin, 0; glucose, 0; red cells, 0.

*May 6, 1902.* To-day the boy is pale, anæmic, facies typhoidal. Tongue slightly furred, edges coated, tremulous. Temperature, 102.8°; pulse small, regular, rapid, 150 to minute. Right tonsil no longer swollen, and not red. Cervical glands not swollen. Gums not spongy. The patient's mother stated there had been "no bleeding during the three days since first visit, but yesterday the bowels moved every half-hour and the movements were black and watery," and the patient complained of pains in the abdomen.

*8th.* The patient's mother visited the dispensary and reported that "his throat was sore," and that there was some swelling on left side of neck; the pulse quiet and slow and regular; the stools natural; the urine clear and yellow. The "black and blue" spots were still present.

The parents would not permit entrance to a hospital, even though unable to keep the boy in bed. The swelling on "left side of neck" proved to be on both sides, due to the heaving-full pulsation of cervical vessels so often seen in severe anæmia.

*13th.* The purpuric spots had disappeared. Color pale lemon yellow, similar to that of pernicious anæmia in adults. Gums pale, firm, and no longer bleeding. Temperature, 100°; pulse, 96, soft, fair, volume regular. Has spat up a small amount of bloody sputum, but no dark stools and no dark urine during the last few days. Throat no longer sore. No enlarged glands in neck.

*17th.* He visited the dispensary. The pallor was marked, the eyelids purple, conjunctivæ pearly. Tongue and throat clear and normal. Temperature, 100°; pulse soft, regular, not dicrotic, 140 to minute. *Heart* showed no enlargement. Apex in fifth

space well inside nipple line, 8 cm. from midsternum. Systolic murmur over apex and base.

No definite spots over trunk or limbs, but a peculiar bluish, mottled appearance over upper thorax and shoulders in front. No glandular enlargement. No enlargement of spleen.

*Blood Examination.* Coagulation time three and a half minutes (Wright). Fresh blood: red cells pale. Plates practically absent. Hæmoglobin, 20 per cent. (von Fleischl); red blood corpuscles, 1,300,000; index, 0.76; white blood corpuscles, 4000.

Red cells: slight poikilocytosis; anisocytosis absent; polychromatophilia slight; erythroblasts not found. Differential (500): polynuclears, 22 per cent.; lymphocytes, 66.5 per cent.; large mononuclears, 11.5 per cent.

*Serum Reaction.* Widal's negative 1 to 60 in three hours.

19th. *Urine Examination.* Pale yellow; clear; acid; specific gravity, 1010; albumin, 0; sugar, 0; casts, 0; red cells, 0. Spectroscopic examination: No blood derivatives.

On May 27, 1902, death occurred. Two days preceding death large purpuric spots appeared over the dorsum of the left foot and about the ankles; the feet and ankles and legs became œdematous, and there was a thin, bloody discharge from the mouth and nose.

The case was treated unsatisfactorily, in that hospital care was not permitted and the patient could not be confined to bed at home. Tincture of iron chloride, iron tonics, arsenic, together with regulation of diet, constituted the treatment. Adrenalin was given for two days from May 6th, and apparently affected the melæna favorably, while later the same drug failed to affect the bleeding from gums and bowel. The slight sore throat was not complained of until after the first inspection, May 3d, although at that time the right tonsil was slightly swollen and red. Under local treatment the tonsil became normal within five days. Careful inquiry in regard to previous diet and surroundings eliminated the possibility of scurvy.

The acute condition, the swelling of the right tonsil, the high percentage of lymphocytes in the peripheral circulation, suggested the possibility of acute leukæmia with an intercurrent infection from the right tonsil, giving rise to well-marked leukopenia. Other sources of infection, such as otitis media, hemorrhoids, pyorrhœa alveolaris, were carefully looked for and not found.

The decrease in leukocytes in leukæmia from 100,000 to 30,000 to 4000, or even lower in some of Cabot's cases, has occurred, so far as I am aware, only in cases with a severe intercurrent infection, such as pneumonia, empyema, septicæmia.

The evident absence of tonsillitis before admission, the sore throat occurring a few days later; the absence of pallor at any period preceding the first severe epistaxis; absence of glandular and splenic enlargement; the persistent bleeding from bowel, gums,

and nose; the purpuric eruption from the onset of the condition, suggests Werlhof's disease rather than acute leukæmia.

From the character of the lymphocytes found in the two blood examinations leukæmia seems excluded. Specimens from three cases of undoubted acute leukæmia examined in the laboratory show the large lymphocytes with "azur-granules" (erythrophilic, but not acidophilic)—Türk's lymphoid marrow cell<sup>1</sup>—in high percentage, and this type of cell was not found in this case, the mononuclear cells being of the lymphocyte and large mononuclear types found in normal blood.

A post-mortem examination was not permitted.

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## TWO CASES OF CHRONIC SPLENIC ANÆMIA (TWIN SISTERS), ONE WITH ACHYLIA GASTRICA.<sup>2</sup>

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THE term splenic anæmia was first used by Griesinger to describe a condition characterized by a severe anæmia associated with chronic enlargement of the spleen. Since Gretscl reported the first case in 1866, an extensive literature has accumulated. An analysis of the cases leads to the conclusion that various diseases have been reported under this name. Some are undoubted cases of pernicious anæmia, others of pseudoleukæmia. In some it would be difficult to exclude malaria, syphilis, and tuberculosis. Banti was the first to make this a primary disease of the spleen. He believes that the enlargement of that organ precedes the anæmia, and that in the later stages the liver becomes cirrhotic; there is jaundice and ascites, eventually leading to death. But whether Banti's disease is a true splenic anæmia, or a cirrhosis of the liver beginning in the spleen, or whether the infantile pseudoleukæmia of von Jaksch belongs in this category, or whether primitive or primary splenomegaly, splenic pseudoleukæmia, Gaucher's endothelioma of the spleen, splenic cachexia, etc., and splenic anæmia are the same thing, or different stages of the same thing, are still mooted questions.

The term splenic anæmia is objectionable, as it assumes a causal relation between the splenic tumor and the anæmia. Objections,

<sup>1</sup> Cells resembling Türk's lymphoid marrow-cells, excepting the "azur-granulation" which Türk states he has not observed in these cells, although he suggests the possibility of the occurrence of such granules in the basophilic protoplasm of an "old" lymphoid marrow-cell. Türk, *Vorlesungen über klinische Hämatologie*, 1904, p. 366.

Read at the annual meeting of the New York State Medical Society, January 31, 1905.

however, can be raised against every proposed substitute. In fact, the entire subject is yet in the stage of discussion. Wentworth, in a comprehensive review on the subject, concludes: "That the blood changes in the so-called splenic anæmia are those of a secondary nature." Also, "that it has not been confirmed that the splenic alterations are primary."

Rolleston, in a discussion on the pathology of splenic anæmia at the seventh annual meeting of the British Medical Association, said: "The fact that mistakes have been made, and from the difficulties presented by some cases will probably continue to be made, in assuming that splenic anæmia explains the morbid condition present in a given case does not prove that there is not a morbid entity, which, as it conforms to no other known type, must, at present at any rate, be tentatively recognized." Senator, during the same discussion, said: "I am of the opinion that so-called splenic anæmia cannot be strictly separated from similar affections of the hæmopoietic viscera which have a great resemblance to leukæmia without the characteristic condition of the leukæmic blood, and which, therefore, it is justifiable to class together under the name pseudoleukæmia, as Connheim proposed in 1865."

Osler, who has done much to give splenic anæmia its standing, and who has reported 18 cases, says: "A special malady does exist, of unknown etiology, characterized by a chronic course, enlargement of the spleen, anæmia of a secondary type, a marked tendency to hemorrhage of the stomach, and a liability in the late stages to be associated with jaundice, cirrhosis of the liver, and ascites." He also says: "It seems probable that the conditions separately described in the literature as primitive splenomegaly, splenic anæmia, splenomegalic cirrhosis of the liver, or Banti's disease are stages of one and the same malady."

It is my purpose to place on record 2 cases of chronic splenic anæmia occurring in twin sisters. The first case I did not see. I am indebted to Dr. Wallace for the notes. The second case was referred to me by Dr. Wallace. I have had the patient under observation since September.

CASE I.—Mrs. J. H. H. when a child had frequent attacks of pain and enlargement of the joints; otherwise she was well up to her twenty-second year, when she was married. This was in 1892. She then weighed 128 pounds. Within six months her weight dropped to 105 pounds, and her general condition was poor. During 1893 she suffered from chronic diarrhœa and soreness in the left side. In 1895 she gave birth to twins. One child (male) was born dead, the other (female) lived three weeks. When two weeks old, rapidly growing, red, sessile tumors, as large as a hen's egg, formed on the posterior surface of the elbows. There was no rash or other abnormality.

In 1898, while at Grace Hospital, Toronto, where she expected

to have a lacerated perineum repaired, an enlargement of the spleen was discovered. Her general condition was poor, and an operation deemed inadvisable.

During 1899 she was anæmic. The ankles were enormously swollen.

Examination February 6, 1900, showed considerable improvement. Her weight was now 130 pounds. The lungs, heart, and pelvic organs were normal.

Abdomen large and distended by a mass which occupied the entire left side, extending below the crest of the ileum, and beyond the middle line. It was hard, smooth, slightly movable, and notched on the anterior border; the liver was not enlarged; there was no ascites.

Urine, cloudy, 1025, acid, large amount of albumin.

Blood, hæmoglobin, 75 per cent.; red corpuscles, 4,320,000; white cells, 850 per cubic mm.

In May, 1900, she had a severe attack of stomatitis. The gums were ulcerated; the submaxillary glands were painful and swollen.

The temperature ranged from 101° to 103°. There was no change in the abdominal findings. The urine was free from albumin.

Blood, hæmoglobin, 30 per cent.; red blood cells, 3,072,000; white cells, 1300. During July and August of that year her condition was wretched. She was emaciated, weak, and had a running temperature. Her death was expected. In the fall she began to improve, and in December she felt quite well and strong, and left the city.

On June 29, 1901, she was in the city for a day. Her condition was fair. Her skin was sallow, with irregular large brown spots. The tumor was about the same.

During the summer of 1902 she passed some renal calculi. In October she had another attack of stomatitis. The submaxillary and cervical glands were painful and enlarged. Her temperature ranged from 100° to 104°. There was some dulness at both apices. Sputum negative. From now on her condition grew worse.

Examination December 22d showed much emaciation. Blood, hæmoglobin, 35 per cent.; red blood corpuscles, 2,100,000; white blood cells, 1200. Differential count, polymorphonuclears, 35.5 mononuclears, 66.5. Sputum negative. She complained of pain in the lower part of the abdomen (right side). There was nausea. The breath was foul. Sputum and stools streaked with blood.

*December 27th.* During the afternoon she was suddenly taken with excruciating pain in the lower part of the abdomen. The abdomen was tender; pulse ranged from 100 to 140; temperature, 102°.

*28th.* Gradual failing of the cardiac and respiratory functions. Death occurred at 9.15 A.M.

*Autopsy* made by Dr. W. H. May at 11 A.M. Body much emaciated, rigor mortis present. There was a little dark yellow subcu-

taneous fat. The diaphragm reached to the third costal cartilage on both sides.

*Chest.* Pericardial sac contained about two ounces of fluid. The heart was apparently normal; weight four and one-half ounces. There was no fluid in the pleural cavities; the right lung was adherent at the apex and along the right border. The left lung was slightly adherent.

*Abdomen.* Full of pus below the mesocolon. No evidence of fat necrosis or venous thrombosis. Small intestine and cæcum injected, matted together, and covered with lymph. Mesenteric glands enlarged. The mucous surface of the alimentary tract apparently normal. Appendix, one and one-half inches long, thick, dark, inflamed, and adherent, but not perforated. Stomach free on both surfaces; no evidence of ulceration. The spleen occupied the entire left half of the abdomen, and was adherent to the diaphragm. It weighed a little over two pounds. There was no pus near it. Right kidney apparently normal; not dilated. It contained a calculus, about the size of an almond; also much sand. The ureter was about the size of the little finger, and about its middle there was a calculus as large as a bean. The left kidney was apparently normal. The suprarenals were small, dark, and friable. The liver was apparently normal. It weighed two and three-quarter pounds. The pancreas and pelvic organs were apparently normal.

Nothing was found to account for the pus, unless it was the appendix. It is safe to assume that it was the result of an acute process and had nothing to do with the chronic condition.

Dr. H. S. Steensland, Director of the Pathological Laboratory of the College of Medicine, Syracuse University, examined sections of the spleen, and reported a marked increase in the amount of reticulum, especially in the splenic pulp, but to a certain extent also in the lymph nodules. Endothelial cells filling the pulp spaces, as observed in the cases described by Gaucher, Bovaird, Harris, and Herzog, etc., were not present.

CASE II.—Miss M., nurse, aged thirty-one years. Father died at sixty-two years of some stomach trouble. Mother is sixty-four years old, and well. Four brothers and three sisters are living and in good health. One sister died at thirty-eight years of peritonitis. One sister (twin) died at twenty-nine years (Case I. of this paper). In 1880 she had measles. From the fourteenth to her seventeenth year she was troubled with lumps or swellings on the hands, knees, and feet. After menstruation set in they almost entirely disappeared. In September, 1898, she had an attack of pleurisy, with effusion. In July, 1898, she had a severe attack of diarrhœa, which lasted about four weeks. At this time she also complained of soreness in the left hypochondriac region. The pain persisted about two months after the diarrhœa ceased. She then entered the training-school for nurses at the Hospital of the Good Shepherd. Hospital work agreed

with her. She gained in weight. Her color was good, and she was known as the rosy-cheeked nurse.

In January, 1899, she left the hospital to nurse her sister. In August of that year she had a second attack of soreness in the left side. Dr. W. L. Wallace examined her, but could find no apparent cause for it. The attack lasted some weeks and then disappeared.

For the next two years she was in indifferent health. At times she felt fairly well and strong; at other times she felt run-down and weak, and was forced to keep to her bed. In June, 1902, she again entered the hospital training-school. The work proved too much for her, and, after being on duty for two weeks, she was forced to turn patient, suffering from swelling of the left knee, left elbow, and right large toe. The diagnosis of inflammatory rheumatism was made. After two months' illness she was able to leave the hospital. Change of scene brought about a marked improvement in her condition. About the middle of September she again undertook to nurse her sister. This she did until the latter's death, December 28th. She endured considerable physical as well as mental strain. During 1903 her condition was poor. She was anæmic, had pains in the extremities, also in the left hypochondriac region. She had occasional attacks of diarrhœa. At other times she was constipated and suffered from sharp attacks of colic. She also had several attacks of stomatitis. The gums would become red and swollen. She also had a mild fever during the attacks.

In November, 1903, while visiting in Toronto, Canada, she consulted Dr. Cotton. He examined her, but could not determine any splenic enlargement. He found some thickening in the region of the appendix and advised an operation. This she declined, and returned to Syracuse. Her condition again improved.

In February, 1904, she had an attack of quinsy. The convalescence was very slow. The soreness in the side continued. A blood examination made by Dr. Wallace showed hæmoglobin 70 per cent.; red blood corpuscles, 3,680,000; white blood cells, 3600; differential count, polymorphonuclears, 17.5 per cent.; lymphocytes, 46 per cent.; large mononuclears, 32.5 per cent.; eosinophiles, 4 per cent.

In July she again visited Canada, and again consulted Dr. Cotton, and now for the first time he discovered that the spleen was enlarged, and advised splenectomy.

In October she returned to Syracuse and consulted Dr. Wallace, who kindly referred her to me.

Patient is thin, but not very anæmic. On the face there are a number of irregular brownish spots. The mucous membranes are of fairly good color. Tongue coated.

Lungs normal; heart not enlarged; sounds accentuated, but no murmurs. Pulse of moderate volume; some arrhythmia. The stomach does not reach below the navel. The liver dulness begins



at the fourth rib. The lower border is just palpable at the free border of the ribs, but is not enlarged.

The spleen is freely movable, and extends three fingers' breadth below the free border of the ribs. It is firm, smooth, and notched on its anterior border.

The right kidney is freely movable. The left kidney is also movable, but to a lesser degree. None of the glands are enlarged. There is some tenderness over the sternum; none over the other bones.

The blood examination shows a mild anæmia of the chlorotic type. Hæmoglobin, 80 per cent.; red blood cells, 4,800,000; white cells, 1600. The differential count shows polynuclear neutrophiles, 13 per cent.; lymphocytes, 46 per cent.; large mononuclears, 40 per cent.; eosinophiles, 1 per cent. No poikilocytosis; no nucleated reds, but some inequality in the size of the erythrocytes.

A blood count, made October 15th, resulted: Hæmoglobin, 70 per cent.; red blood corpuscles, 4,700,000; white cells, 600. There were so few white cells that it was difficult to make a differential count. It was, however, very evident that the mononuclear cells far outnumbered the polymorphonuclears.

On account of the frequent attacks of diarrhœa, I determined to make an analysis of the stomach contents. She was given the ordinary Ewald test-breakfast, consisting of 300 c.c. of water and 50 c.c. of bread, and the contents aspirated one hour later. The obtained contents formed a thick, gelatinous mass, consisting of much mucus mixed with the food particles. The bread was not well digested. A chemical examination revealed that free hydrochloric acid was entirely absent, the total acidity was 4. There was neither pepsin nor rennet present. Two days later I gave her a test-meal consisting of soup, meat, bread, and vegetables. Four hours afterward the contents were aspirated. The thick, gelatinous mass passed through the tube with difficulty. Macroscopically the various ingredients of the meal could be distinguished. An analysis gave the same result as before. No free hydrochloric acid, no pepsin, no rennet, and a small amount of combined acids.

Since then I have made repeated examinations of the stomach contents, at various times of the day and under varying conditions, and each time with the same result—a complete absence of free hydrochloric acid and the ferments; in other words, a true achylia gastrica.

Repeated blood examinations were also made. The result was always about the same. The red cells varied from 4,100,000 to 4,800,000, the whites from 600 to 2700. The differential counts, likewise, gave similar results. The polynuclear neutrophiles were always in the minority. The highest polynuclear count was 30 per cent.; the lowest 11 per cent. At no time were there any myelocytes or nucleated reds present, nor was there any poikilocytosis. In estimating the white cells the Türk counter was used, the entire chamber,

equivalent to nine ordinary Thoma slides, being counted. In the differential counts I followed Türk's classification of the white cells. The transitionals were counted with the large mononuclears, while under lymphocytes, both large and small lymphocytes were included.

These cases present some interesting features. First, the presence of the disease in twin sisters. Bovaird, Brill, Collier, Wilson, Springthorpe, and others have reported instances of splenic anæmia occurring in more than one member of a family. Whether this is merely a coincidence or the result of an infection or of some congenital predisposition cannot be positively asserted. Little is known of the etiology of the disease. Micro-organisms have been searched for, but no specific germ has been isolated. The disease resembles a toxæmia. Whether the toxin is produced in the spleen or gastrointestinal tract cannot in the present state of our knowledge be answered. The fact that improvement and even cure have followed splenectomy would indicate that the spleen plays a responsible part. However, it is generally believed that the gastrointestinal tract is the source of the poison.

The marked leukopenia is also noteworthy. In Case II., one count showed but 600 white corpuscles per cubic millimetre. Here, also, the question might be raised; are we dealing with a process of cell destruction or with a disturbance of cell production? We know that hæmolysins and leukotoxins are produced in the blood. But we are not familiar with the production of auto-hæmolysins or auto-leukotoxins. The differential counts in both cases were a little unusual. Ordinarily, in splenic anæmia the differential count shows nothing characteristic. In both of these cases there was a marked relative as well as absolute decrease of the polymorphonuclear cells, and a decided relative increase of the large mononuclear leukocytes.

Another interesting feature is the stomach findings in Case II. We have the condition known as achylia gastrica (Einhorn). The continuous absence of free hydrochloric acid and the ferments in the gastric contents. Achylia gastrica is frequently associated with pernicious anæmia. In fact, the absence of free hydrochloric acid is more frequently associated with this disease than with any other, not excepting cancer of the stomach. The relation of the stomach mucosa to the blood condition has been much discussed. It is safe to say that both are due to the common toxic agent and do not bear the relation of cause and effect to each other. A short time ago Nothnagel called attention to atrophy of the intestinal mucosa as the cause of pernicious anæmia. Faber has recently investigated this question. He concludes that in pernicious anæmia there is no change either in thickness or the character of the intestinal mucosa. He ascribes Nothnagel's findings to post-mortem changes. Whether achylia gastrica is only a coincidence in this case, or whether it is as common with splenic anæmia as with pernicious anæmia, the examination of the stomach contents in other cases will show.

Both cases also show a marked tendency to periods of remission, during which there is a decided improvement of the symptoms. Such periods of remission are quite common in the diseases of the blood-producing organs, like pernicious anæmia, leukæmia, and pseudoleukæmia.

The effect of arsenic in Case II. was rather striking. The patient had at various times taken the drug—each time with a marked aggravation of the symptoms. The lowest white count was encountered while she was taking Fowler's solution. This corresponds with the known physiological action of arsenic, namely, that it stimulates the production of the erythrocytes, while it inhibits the formation of the white cells. Walter Broadbent has called attention to the dangers of the indiscriminate use of arsenic. He believes that many symptoms, like pigmentation of the skin, œdema, ascites, and the sensory disturbances of pseudoleukæmia, leukæmia, and pernicious anæmia are due to the arsenic taken.

The question of operation must be considered in these cases. In some cases splenectomy has brought about a cure; in others it has prolonged life. Knowing the powerlessness of drugs, the knife may be appealed to in suitable cases, even though its use is purely empirical.

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## A CLINICAL AND PATHOLOGICAL REPORT OF A CASE OF SPLENIC ANÆMIA.

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AND

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1. CLINICAL REPORT (Dr. Sanford). *Case of anæmia of long duration with gastrointestinal disturbances and pain in splenic region; recent severe and repeated hemorrhages by stool and vomitus following traumata; blood characteristic of secondary anæmia of chlorotic type without leukocytosis, with no general lymphatic enlargement; idiopathic splenomegaly; exploratory laparotomy; subsequent splenectomy; death.* Mr. B. R. T., aged twenty-eight years, married, a farmer, of Greenwich, Ohio, was sent to Lakeside Hospital on the evening of October 14, 1903, with symptoms of vomiting of blood, tarry stools, profound anæmia and a tumor in the lower mid-abdomen.

The patient stated that three weeks before he had been thrown over the head of a spirited horse and had struck flat on his back, but had not been prevented from working about as usual. Two

weeks later, which was a week before entrance, he was jerked off his feet and thrown violently some distance by this same horse which he was leading. The following morning he had a copious black liquid stool, after which he vomited much blood, he thinks at least a pint, of both dark blood clots and some fresh blood. This vomiting continued at intervals that day, and then stopped, but he had large tarry stools nearly every day up to the time of his entrance. He was in bed during most of the time, felt greatly prostrated, and had no appetite.

His physician on the day before he was brought to the hospital first noticed a tumor in the lower mid-abdomen, which he took to be a distended bladder, but on catheterization its size was not altered. The urine appeared normal and contained no blood. Dr. Maynard, of Elyria, who was called in consultation, then sent him to the hospital. On entrance the patient seemed greatly fatigued from his journey and could answer questions with difficulty.

*Physical Examination.* Patient is a young American, slight in frame, very sallow, somewhat emaciated, in considerable state of shock. Temperature, 100.6°; pulse, 120, small volume, regular, compressible; respiration, 28.

Sclera subicteric; teeth poor; tongue furred and moist.

Chest, slender and shallow, expansion equal and good; clavicles and ribs prominent; supraclavicular and infraclavicular fossæ deep; no glands palpable. Interspaces sunken; epigastric angle narrow.

Percussion note dull over clavicles and supraclavicular spaces, elsewhere hyperresonant. Breath sounds clear front and back; musical rales on expiration in left foreaxillary line.

The area of cardiac dulness is hard to define; it apparently extends somewhat to the right of the sternum; a blowing systolic murmur is heard all over the base, and not at the apex or in the axilla.

The abdomen is sunken, scaphoid in general outline, somewhat sensitive to palpation in the left upper quadrant where there is slight muscular rigidity. Liver dulness begins at the fifth space in nipple line and extends to costal margin. Splenic dulness not made out. The pole of right kidney is palpable on deep inspiration. Left kidney not felt, and it seems with one hand in the left lumbar region and the other under the left costal margin that the two hands can be brought nearer together with less intervening structures on the left than on the right side. On pressure here the patient is evidently sensitive, although apathetic to examination elsewhere. Just below the umbilicus is a mass, oval in general outline, lying diagonally, its higher pole to the right, smooth, hard, not tender, quite freely movable, edges rounded, no notches felt. The abdomen is everywhere tympanitic except over the mass described where the note is flat.

The inguinal glands are slightly enlarged. Rectum empty except for a few small clots; no hemorrhoids; extremities thin; no tibial scars or œdema.

The patient was given artificial heat and stimulation by strychnine and saline subcutaneous infusions every six hours. Milk and whites of eggs; morphine for restlessness. A glycerin enema resulted in a black liquid stool, which on examination was found to be largely decomposed blood.

The immediate history of severe repeated traumatisms combined with the patient's statement that he had always been well previously, quite naturally led one to regard the present symptoms as the direct result of the injury rather than to seek a more remote cause. Various possibilities were considered, among which hemorrhage from a gastric or duodenal ulcer, and a dislocated viscus were foremost. Neither diagnosis seemed to account for all the symptoms, and in view of the later developments in the case, a further discussion of these points is unnecessary.

The patient reacted fairly well to stimulation, and was kept under observation the next day, during which he had seven more black liquid stools. Rectal feeding was added to the treatment which was otherwise the same.

A blood examination on the day after admission showed: Reds, 2,800,000; leukocytes, 8000; hæmoglobin, 25 per cent.; coagulation time 45 seconds; no plasmodia seen.

The next day the patient's unchanged condition and the uncertain diagnosis seemed to warrant an exploratory operation which was decided upon.

*Operation, October 16th* (Dr. Dudley P. Allen. Gas and ether). *Laparotomy; exploration.* An incision 9 cm. in length was made in the median line below the umbilicus and over the tumor. A small quantity of clear peritoneal fluid was met with from which cultures were taken. The intestines were normal. The mass was identified as the spleen, greatly enlarged and displaced, freely movable, otherwise of normal appearance. Accurate measurements were not taken, but the organ seemed at least two or three times its normal size. The surgeon considered any operative procedure on the spleen unwise in the patient's condition and closed the incision. Another incision in the median line of the epigastrium was then made and the stomach inspected, and found normal. Nothing abnormal felt about the liver, gall-bladder, appendix, or pancreas. Palpation of the kidneys showed them apparently normal in position and size. The incisions were then closed. The patient received very little shock from the operation, which took but fifteen minutes.

The conditions found at operation raised the question whether the traumata might not be coincidences or, perhaps, exciting causes in producing the appearance of symptoms primarily due to some

as yet unrecognized organic lesion. The arrival of the patient's friends gave the first opportunity of getting the family and previous history in the case, which was as follows:

*Family History.* Father died of "broken back" at the age of seventy years. Mother and one brother living and well. An uncle died of heart disease. No history of malaria, syphilis, cancer or tuberculosis in the family.

*Previous History:* Patient had children's diseases. He has always been pale since childhood. Between seven and eight years ago he had an attack of very violent vomiting which continued all night and was not connected with any indiscretion in diet; vomitus contained no blood. He has always had poor digestion, often distressed after meals, sometimes vomiting, with relief to the discomfort.

In the summer of 1902 he had "bowel trouble," in which there was diarrhœa, griping pains, severe vomiting, with some blood in stools and vomitus. From this time up to the injury the patient was not well, and was under a doctor's care for general "ill feeling" and frequent urination. In the winter of 1902, he also complained of a good deal of dragging pain in the back and left side. No history of venereal disease; tobacco in moderation; no alcohol. Patient has not lived in a malarial district and never had periodic chills.

With this suggestive history and the enlarged and dislocated spleen found at operation, a detailed blood examination was then made and showed the following conditions: Reds, 3,480,000; leukocytes, 8500; hæmoglobin, 25 per cent. Differential count of 600 cells: polymorphonuclears, 74 per cent.; small mononuclears, 18 per cent.; large mononuclears, 4 per cent.; transitional forms, 1.5 per cent.; eosinophiles, 2.5 per cent. Red cells took stain poorly, and were variable in shape and size, centre quite thin, no rouleau formation, some poikilocytosis, six nucleated reds seen; no plasmodia.

The urine was amber, clear, specific gravity, 1020, acid, no sugar, faint trace of albumin, sediment, few leukocytes, epithelial cells.

The case then presented the following data: A patient with (1) a previous history of an anæmic condition with gastrointestinal disturbances and pain in the splenic region; (2) an immediate history of severe and repeated hemorrhages by stool and vomitus following traumatism; (3) a present condition of profound anæmia, with the blood characteristic of a secondary anæmia of the chlorotic type without leukocytosis, with no general lymphatic enlargement; and (4) a splenomegaly apparently not due to malaria, syphilis, tuberculosis, leukæmia, or amyloid disease. From this symptom-complex the possibility of the existence of splenic anæmia was strongly suggested and a course of supporting treatment was instituted while further study could be carried on.

During the week after operation the patient's general condition improved slightly. The stools no longer contained fresh blood,

but were dark, copious, watery, varied between three and seven daily and were at times involuntary. There was no further vomiting. Liquid nourishment was well taken. The temperature ranged between 99.5° and 101.5°, and the pulse from 100 to 140. The outline of the tumor was marked out on the abdomen in silver nitrate solution to watch for changes in its size or position.

On the tenth day after operation the tumor was found to have increased in size by almost one-half, and the gain in size seemed mostly toward the right and below. The new outlines of the enlarged organ were marked on the patient's abdomen. Two days later a still further very rapid increase in size was apparent, so that the anterior surface of the mass presented an area twice as large as when the patient entered the hospital. The incisions of the original exploration were firmly healed by first intention. To-day for the first time petechial hemorrhages were seen on the sides of the chest in areas the size of the palm of the hand, and smaller similar purpuric spots appeared on the right forearm and hand.

No change in subjective symptoms accompanied these new phenomena. The patient was still apathetic and weak, though he declared he felt better, and his only complaint was the exhaustion attendant on frequent bowel movements which still were of a tarry color and averaged five to six daily. The blood condition was examined from day to day, and showed practically the same condition as given above.

The question of splenectomy in the case had been constantly before the surgeon's mind, but he desired first to improve the patient's general condition in view of the recent enormous loss of blood he had suffered. The rapid and sudden increase in the size of the spleen, however, convinced Dr. Allen that ground was being lost instead of gained, and an immediate operation was proposed and accepted by the patient and his friends.

*Operation October 29th* (Dr. Dudley P. Allen. Gas and ether). *Laparotomy; splenectomy; closure.* A vertical incision 15 cm. in length was made separating the fibres of the left rectus muscle in order to avoid the former incisions. On opening the peritoneum some clear fluid was met with from which cultures were taken. The spleen was found to be lying free in the abdomen without adhesions to the intestines or other structures, its only attachment being a large long pedicle containing four twists, composed of large congested vessels, some of which contained thrombi. A more detailed, microscopic description of the organ and its pedicle will be given later.

The pedicle was securely tied high up with silk, clamped off distally and removed with the organ, which was with difficulty squeezed through the skin incision. No hemorrhage accompanied the removal; the pedicle stump was reinforced by over-and-over catgut stitches, and showed the openings of several large vessels.

The abdomen was closed in layers. The patient seemed to receive no shock from the operation which lasted twenty minutes.

For two days after operation the patient's general condition was encouraging. The temperature approached the normal, and the pulse rate decreased to an average of 90, with improvement in its quality. Stimulation with strychnine and saline subcutaneous infusions was continued as before.

On the third day a marked œdema of the whole right leg appeared which increased rapidly to alarming proportions. This was followed some days later by œdema of the right side of the scrotum and left side of the neck. Vomiting reappeared on the sixth day, and it became difficult to nourish the patient, as rectal nutrition was not retained except at intervals. There was no further appearance of blood, however, either in the vomitus or stools. Purpuric areas remained unchanged. Later the vomiting ceased and the patient seemed much brighter again. An attempt was made to give Fowler's solution, but this had to be abandoned, as on the eleventh day the patient again rejected all nourishment. The abdomen, which up to this time had been flat, now began to show distention, with appearance of free fluid in the flanks. This collected rapidly, and on the thirteenth day the abdominal wound, which had healed and from which the stitches had been removed, burst open and a large amount of clear fluid escaped, from which cultures were sterile.

The patient now was irritable and very hard to rouse, sleeping nearly all the time with some delirium. Nourishment was refused, and rejected when given. Stools and urination were involuntary. This condition of progressive weakness, accompanied by emaciation, dyspnœa, and cyanosis, continued until the patient's death on November 15th, seventeen days after operation.

The changes in the blood following the removal of the spleen were very interesting, and in the main coincided with observations reported under like conditions in other cases, though, unfortunately, the patient's death prevented their being followed out over a long period.

Immediately after operation there was a great diminution in the red corpuscles from 3,480,000, four days before operation, to 1,836,000 two days after operation. This could not be accounted for by hemorrhage, either before or during the operation, as there was no great loss of blood immediately before the operation and no blood was lost in tying off the pedicle of the spleen. It must be attributed to the effect of the removal of the organ. After this initial drop the red count began steadily rising and had reached 2,800,000 just before death.

The white count which had been 8500, jumped to 34,000 two days after operation and gradually decreased to 22,000 at death. The percentage of hæmoglobin which before operation was 25 per cent., dropped to 22 per cent. after operation, and then gradually rose to



28 per cent. All these changes, the marked postoperative diminution in red cells, and to a less degree in hæmoglobin, and the sudden rise in leukocytes, corroborate previous experiences following splenectomy.

In the differential counts the polymorphonuclear form showed a marked increase from 74 per cent. before operation to 93 per cent. before death. The eosinophiles varied in amount. Nucleated red forms which averaged 6 in a count of 600 cells before operation increased to 36 before death.

To facilitate comparison the results of the various counts are tabulated below.

	Date.	Red cells.	Leukocytes.	Hæmoglobin.
Before operation . . . . .	October 16	2,800,000	8,000	25 per cent.
	" 25	3,480,000	8,500	25 "
	November 2	1,836,000	34,800	22 "
	" 3	1,914,000	30,000	23 "
	" 7	2,212,000	22,000	22 "
After splenectomy. . . . .	" 10	2,848,000	23,720	28 "
	" 11	2,464,000	26,000	26 "
	" 12	2,568,000	23,000	27 "
	" 13	2,632,000	22,000	28 "
	" 14	2,682,000	22,000	28 "

#### DIFFERENTIAL COUNTS OF 600 CELLS.

	Date.	Polymorpho- nuclear.	Small mononu- clear.	Large mononu- clear.	Trans- itional.	Eosino- philes.
Before operation	Oct. 25	74.0 per ct.	18.0 per ct.	4.0 per ct.	1.5 per ct.	2.5 per ct.
After splenectomy	Nov. 2	83.5 "	12.75 "	1.75 "	1.50 "	0.5 "
	" 7	89.0 "	4.66 "	2.33 "	2.0 "	2.0 "
	" 10	93.0 "	3.8 "	1.4 "	0.6 "	1.2 "
	" 13	92.3 "	3.6 "	1.3 "	1.0 "	1.8 "

2. PATHOLOGY. (Dr. Dolley.) *Autopsy Protocol.* (Autopsy performed seventeen hours after death.) The body is that of a well-formed but emaciated white man, 180 cm. long. There is moderate rigor mortis, and slight posterior hypostasis. The conjunctivæ are somewhat yellow. The mucous membranes are pale. The skin is sallow but not pigmented. A few small petechial areas are scattered just above the costal border. There is no glandular enlargement.

The chest is barrel-shaped. The supraclavicular fossæ and sternal notch are deep. The abdomen is scaphoid. Two recently

healed wounds of operation appear in the midline; one, 6 cm. long, beginning at the xiphoid cartilage, the other, 7 cm. long, beginning at the umbilicus. A third laparotomy wound, healed with the exception of one stitch, 12 cm. long and 3 cm. to the left of the umbilicus, is present in mid-abdomen. The right leg is larger than the left throughout, and moderately œdematous.

*Brain and spinal cord* not examined.

*Abdominal Cavity.* The spleen is absent. The splenic veins become very tortuous from the end of the pancreas, one and one-half coils being left after the splenectomy. They measure from the end of the pancreas to their ligated extremity 2.5 cm. coiled and 5 cm. uncoiled. The apposing surfaces of the coils are united by well-organized adhesions. Beginning at the junction with the portal vein, the splenic vein and its branches become more and more distended with palpably soft material until at their ligated extremity the larger of the two branches is 2 cm. in diameter. The veins are attached to the jejunum at one spot, 2 cm. in diameter, by organizing fibrinous exudate. On incision they contain soft mixed thrombi, which in places are loosely attached to the wall. There is slight thickening of the walls but no evidence of calcification.

The *splenic artery* is rather tortuous and dilated. It measures 2.5 cm. from the end of the pancreas to its ligated extremity. Its elasticity is poor, the intima is somewhat roughened and extremely reddened toward the distal end. It contains a similar grayish-red thrombus.

*Mediastinal fat* is scanty. The *thymus* is absent.

*Pleural Cavities.* Each contains about 10 c.c. of clear serous fluid. There are no adhesions.

The *pericardial cavities* contain 30 c.c. of similar fluid. The sac wall is not thickened.

*Thyroid Gland.* Both lobes are somewhat enlarged. The tissue appears normal.

The *tracheal glands* are markedly anthracosed. One at the bifurcation is studded with small fibrocaseous tubercles.

The *lungs* are voluminous, externally smooth and slightly anthracosed. They are hypercrepitant and cushiony except in the lower posterior portions. On section there is moderate hypostasis of the lower lobes. Elsewhere the tissue is more moist than normal. The left weighs 550 grams, the right 549 grams.

The *bronchi* contain some frothy watery mucus.

The *bronchial glands* are like the tracheal. One is composed of a calcified envelope with a caseous centre.

The *heart* is of normal size. The right ventricle averages 4 mm., the left 15 mm. in thickness. The auricles and right ventricle contain post-mortem jelly clots. Fluid blood is scant. The muscle is pale and flabby. The valves are normal except for a few atheromatous patches on the ventricular surface of the right mitral

segment. The circumferences of the valvular orifices are: aortic, 6.2 cm.; pulmonic, 7.3 cm.; mitral, 9.5 cm., and tricuspid, 13 cm. The coronary arteries have a roughened intima with considerable atheroma. They are not tortuous. The endocardium elsewhere is smooth.

*Aorta.* The elasticity is normal. The wall is not thickened. The intima in places is roughened by yellowish or whitish plaques.

The *pulmonary artery* and *venæ cavae* appear normal.

The *liver* weighs 1356 grams. It measures 27 x 14 x 8½ cm. The left lobe measures 13½ x 14 x 5 cm. It is contracted, but its shape is fairly preserved. The capsule is slightly thickened, and the capsular veins are moderately injected. The veins of the round ligament are not dilated. The surface is moderately roughened and nodular, especially over the inferior and lateral portions of the right lobe. Over the inferior surface are several nodules softer in consistence than the rest of the tissue. On section, the organ is moderately hyperæmic. The cut surface is uneven and finely, though not uniformly, granular. The tissue is firm and cuts with increased resistance, especially in the lower and lateral portions of the right lobe, just under the capsule. The lobular outlines are not distinct; the tissue is markedly bile-stained, of a dirty brownish-yellow color. Owing to the bile staining the character of the apparently increased connective tissue is not evident. Glisson's capsule is most affected.

The *portal vein* is not thickened and its intima is smooth; it is free from thrombi.

The *gall-bladder* is constricted at the junction of its proximal and middle thirds and bent upon itself, so that the two portions are in partial apposition and united by old adhesions. Elsewhere it is non-adherent and apparently normal, containing dark bile. The ducts are patent.

*Æsophagus.* Congested sub-mucosal veins are distinct about the cardiac orifice.

The *æsophageal veins* are considerably dilated and tortuous. The coronary veins of the stomach are not so dilated, but the cardiac branches communicating with the æsophageal veins show marked varicosity.

The *stomach* is somewhat dilated, but the wall is not appreciably thinned. It contains 500 c.c. of brown sour-smelling fluid. The mucosa shows considerable post-mortem change and is not indurated. The sub-mucosal veins about the cardia and along the greater curvature are dilated. The folds of the mucosa only appear along the greater curvature, where their prominence is due to dilated veins. No eroded veins are apparent. There are no ulcers nor scars.

The *pancreas* is moderately hyperæmic. The head and body are of normal size, but are distinctly indurated. The tail is very con-

tracted and firmly attached to the splenic vessels. On section there is great increase of dense fibrous tissue.

The *small intestine* is not distended. It shows only an occasional congested but not swollen area in the mucosa. The veins of the serosa are not congested.

The *appendix* is normal.

*Large Intestine.* The mucosa of the cæcum and the ascending colon is markedly congested. There are no hemorrhoids.

The *suprarenals* show post-mortem softening of the medulla.

*Kidneys.* Right weighs 215 grams, the left 285 grams. They measure respectively 12 x 7.5 x 3.8 and 13 x 8.6 x 7 cm. Perirenal fat is scanty. The cortical veins are not dilated. The capsule is normal.

The cortex of the right is 6 mm., of the left 8 mm. in thickness. The cut. surface is smooth, but mottled with grayish areas corresponding to the labyrinths. The organs are moderately pale and the glomeruli are barely visible. The arteries are not sclerotic.

The *ureters, bladder, seminal vesicles, prostate, and testicles* appear normal.

The *mesenteric glands* are small and barely palpable.

The *retroperitoneal glands* are enlarged, firm, and of a glistening grayish-white appearance on section.

*HæmolympH Glands.* Lying on both sides of the sternum, along the carotid arteries, the renal vessels, the iliac vessels, and about the splenic vein and the œsophagus appear glands varying in size from a pinhead up to that of a large bean. These are soft, dark-red, spleen-like and fairly abundant. Between thirty and forty of convenient size were removed.

The *right iliac vein* just above Poupart's ligament is filled with a red, non-adherent thrombus.

The *right femoral vein* contains a similar thrombus. This changes in character 5 cm. below Poupart's ligament, having a white friable core which at one point is attached to the wall.

The *inferior hemorrhoidal veins* are moderately dilated and tortuous.

*Bones.* Several ribs and the right femur were opened and found to contain bright-red and succulent marrow. No lymphoid areas appear.

*Spleen* (received from the surgical department. Gross description by Dr. Howard). The specimen consists of a spleen, irregularly oval in shape, presenting a rounded anterior margin from which the notch has been obliterated. It weighs 1650 grams and measures 22 x 16 x 7 cm. The vessels, which form a pedicle, are covered with fine pinpoint fibrin masses, but present no adhesions. This pedicle is twisted four times, and its uncoiled state measures 17 cm. in length and 4 cm. in its greatest diameter. It is composed of several large tortuous veins surrounded by a considerable amount of fat,

and several branches of the splenic artery, which is divided a considerable distance from the hilus. The pedicle also includes a soft body measuring 1.5 x 1 cm., covered with peritoneum, and resembling an enlarged lymphatic gland. At the distal end mixed gray and red thrombi protrude from the veins. The largest vein is 2.5 cm. in its greatest diameter. On incision they are filled with thrombi, but contain a variable amount of thin fluid blood. The thrombi are partly red and partly mixed, some being yellowish-gray in color. As a rule they are non-adherent, or can be easily separated. In general the mixed thrombi are soft or friable. The thrombi can be readily traced into the large and the small veins of the organ. The walls of the veins are not much thickened, and show no signs of recent or old inflammation except the thickening of one near the hilus.

The splenic tissue is light brown in color and œdematous. The trabeculæ are well marked, the lymph nodes obscure. The tissue is not friable. There are no infarcts.

*Microscopic.* Material from all organs was hardened in Zenker's and Orth's fluid, in formalin and in alcohol, and stained by ordinary and special methods.

*Lungs.* There is moderate emphysema and anthracosis. The sections from the posterior portions show moderate congestive œdema. The bronchi and pulmonary arteries are normal. Careful search for the bone-marrow giant cells described by Warthin in his cases was negative.

*Heart.* There is marked segmentation and some fragmentation of the muscle.

*Liver.* The connective tissue is moderately increased, but not at all uniformly even in the same section. The increase is greatest in the right lobe under the capsule, as noted macroscopically, Glisson's capsule about the larger vessels being particularly thickened. The lobules are usually sharply defined, but occasionally the connective tissue extends somewhat into them. The connective tissue is dense fibrous in character, with few nuclei, and slight round cell infiltration. In places of more marked fibrosis, fibroblastic cells are more abundant, but the tissue is nowhere actively proliferating. More rarely an increase of fibrous tissue about the central veins is noted. Mallory's connective-tissue stain shows here and there a slight increase of the reticulum of the lobules. This is more prominent in areas of atrophy of the lobular centres. This reticulum takes a light red with Van Gieson's stain. A very few fibroblastic cells appear in these areas and several capillaries are filled with proliferating endothelial cells with a few karyokinetic figures. Excepting these few instances endothelial proliferation does not occur. In the more cirrhotic portions many lobules show dilatation of the central veins and capillaries with some atrophy of the liver cells, but this is appreciable in but few lobules in the less fibrosed

areas. The atrophic liver cells present more or less fatty degeneration and necrosis, with a little brownish-yellow pigment. Numerous attempts to demonstrate the presence of iron were unsuccessful. Proliferation of bile canaliculi is found in only two areas. No bone-marrow giant cells are found.

The *stomach* and *intestines* show chronic passive congestion, associated in the small intestine with slight chronic catarrhal inflammation.

*Pancreas.* Sections from the head and body show a moderate increase of connective tissue, both perilobular and interacinous. Some islands of Langerhans also have an increased amount of stroma. The sections from the tail show marked fibrosis, dense fibrous and hyaline tissue replacing many lobules, while the remaining ones are small and distorted. The ducts have a thickened wall and a few are tortuous. The islands of Langerhans are diminished in number. A few are unaffected. In some there is fibrosis, but in others fatty and granular degeneration of the cells is more pronounced. The veins are moderately congested and have thickened walls, particularly in the tail.

The *kidneys* show a very slight chronic interstitial nephritis. There is no deposition of pigment.

The *portal* vein is normal.

*Splenic Veins.* The intima is slightly and irregularly thickened and is composed of dense fibrous tissue with few nuclei. Thickening of the adventitia is more pronounced. In the latter, particularly about the vasa vasorum, there is moderate fibroblastic proliferation. But few fibroblastic cells occur in the intima and media. Organization of the thrombi is well advanced in places.

The *mesenteric glands* are fibrosed. There is some proliferation of the endothelium.

*HæmolympH Glands.* A few are of the marrow lymph type described by Warthin, but show partial transformation into ordinary lymph glands. The lymph spaces are full of endothelial cells, some of which are phagocytic for red blood and lymphoid cells. Only a moderate number of bone-marrow giant cells appear.

The majority of the hæmolympH glands resemble splenic tissue in structure. The follicles contain no germinal centres and usually show small hyaline areas. The blood sinuses, which are much dilated, are only partly filled with blood. The most striking feature is the presence within them of numerous large cells of endothelial type packed with red blood cells. Mononuclear eosinophiles appear in great numbers, and normoblasts are moderately numerous. A few mastzellen are present. Numerous cells resembling myelocytes appear in the blood sinuses, but these are more abundant in the lymph spaces of the glands of marrow lymph type (Wright stain). Pigment is in moderate amount. It gives the iron reaction with

ferrocyanide and HCl. Some phagocytic cells give the same reaction in a diffuse way.

The *bone-marrow* (rib) is of a poor lymphoid type. Giant cells are not apparently reduced in number. Plasma cells and polymorphonuclear leukocytes are in small proportion, but mononuclear eosinophiles with nuclei varying greatly in size are extremely abundant. Polymorphonuclear eosinophiles, while absolutely increased, are less numerous relatively. Normoblasts appear in large numbers with active mitosis. Myeloblasts are only occasionally seen. Neutrophilic myelocytes are almost entirely absent. A peculiar feature with the Wright stain is the presence of cells resembling lymphocytes, but with a red protoplasmic border. Excluding these, ordinary lymphoid cells are not increased in number.

There is a scanty amount of iron containing pigment, both in cells and free.

*Spleen.* The capsule is moderately thickened and composed of a dense hyaline connective tissue. The trabeculæ are also thickened and are farther apart than normal. The splenic tissue is constructed of considerably dilated blood spaces, more or less filled with blood, and separated by a moderate amount of usually dense fibrous tissue with a varying number of fibroblasts. Under the capsule this newly formed connective tissue is much more abundant, and it is not uniform in the other sections, thick fibrous bands appearing here and there. Hyaline transformation of the connective tissue appears nowhere outside of the trabeculæ proper. The venous spaces are lined either by an almost flat or a somewhat swollen endothelium with an occasional free cell, but no proliferating endothelium appears. Scattered through the pulp are relatively few lymphoid cells and an almost equal number of polymorphonuclear leukocytes. The lymph nodes are farther apart than normal, but it is not possible to say they are absolutely diminished in number. They are usually not atrophic but show an increase of coarse reticulum with a few fibroblasts. Often the central arteriole is thickened and hyaline. The veins are greatly dilated, their walls are moderately thickened and many contain fibrinous and mixed thrombi. Not infrequently small fibrinous clumps appear in the blood spaces.

A very moderate amount of pigment is deposited in phagocytic cells in the blood spaces or in the stroma or lies free in the trabeculæ. It gives the iron reaction. A few normoblasts, plasma cells, and mononuclear eosinophiles are to be seen, but neither myelocytes nor bone-marrow giant cells are found.

With the Van Gieson stain there is considerable variation, but a large part of the newly formed stroma takes a deep-red color. A section through one of the splenic veins removed at operation shows the same degree of fibrous thickening as in the stump. The

adventitia is the seat of a much more marked fibroblastic proliferation. The thrombus is just beginning to organize.

*Pathological Summary.* There is nothing in the histological structure of the spleen which cannot be explained simply by chronic passive congestion. In the causation of this, two factors have to be considered—*i. e.*, the abnormality of the splenic vessels and the cirrhosis of the liver. The dislocation of the spleen must have been of long standing, for the splenic vessels uncoiled measured 19.5 cm. from the end of the pancreas. Granting even that the multiple twists all occurred as a result of the accidents, which is hardly probable, the elongation which existed prior to this must have caused considerable interference with the splenic circulation.

In two cases of splenic anæmia, reported by Dock and Warthin, there were stenosis and calcification of the portal vein, a condition identical with this one as far as the effect on the spleen is concerned. The question they raise is whether the portal lesion is primary and the splenic fibrosis secondary to it, or, on the other hand, whether the splenic condition is primary, while the condition of the portal vein is coincidental or results from a toxic condition of the portal blood dependent upon the disturbed splenic function or dependent upon a portal or general intoxication. The dislocation of the spleen could not have been of congenital origin, for the alteration does not indicate such a long-standing condition, and an enlargement of the organ at once suggests itself as the main factor in its production.

The abnormality of the splenic vessels is essentially a mechanical, not an organic one. Granted that some enlargement of the spleen, from whatever cause, started the elongation of the splenic vessels, once produced, with probably some torsion, the reaction on the circulation of the dislocated organ would be so great that the subsequently increased congestion and fibrosis would result largely from the condition of the vessels. The condition of the spleen must be considered then as largely secondary to that of the vessels, which gives them a very probable etiological significance. If splenic anæmia existed before the dislocation of the spleen, and the initial enlargement and the dislocation of that organ were manifestations of the pathological processes of the disease, the splenic vessels lose their casual relationship. But the histological structure offers no evidence of this. There is not even the proliferation of endothelium so commonly found in the spleen in this disease to complicate the picture.

The relationship of the cirrhosis of the liver to the condition in the spleen presents the greatest difficulty in interpretation. In part the process in the liver is regarded as a mild and not uniform chronic passive congestion, with a just beginning central cirrhosis, shown by the increase of fine reticulum in the atrophic portions of the lobules, with some endothelial proliferation. The moderate emphysema of the lungs offers a probable explanation for this



condition. More important there is also a moderate though irregular increase of periportal tissue, but the histological pictures of the fibrosis in the liver and in the spleen are too nearly identical to draw conclusions regarding time relationship. What part the liver played in the production of the splenic condition it is impossible to say. Was the hepatic process primary, and was the initial enlargement of the spleen leading to its dislocation secondary to it, or were the two processes coincident? The fibrosis in the liver and in part that in the spleen may have resulted from a general or portal intoxication.

The changes in the hæmolymp nodes are interpreted as compensatory for the failing splenic function. It is probable that the bone-marrow shared to some degree in the assumption of this function. But the presence of pigment and phagocytes in the spleen would, however, indicate that this function was not entirely lost, while the moderate evidence of old hæmolysis in the hæmal glands would further bear this out. But these glands show an excessive number of phagocytes full of intact red blood cells which is readily explained by the results of Warthin's work. He concludes from his experiments with sheep that hæmolysis and leukocyte formation are the functions taken up by the hæmal glands after splenectomy. But the hæmolytic action of these glands exceeds that of the normal spleen, and the resulting anæmia is compensated for by increased activity on the part of the bone-marrow. The marked fall in the blood count after splenectomy was due then to this excess of hæmolympatic hæmolysis over that of splenic.

No iron pigment could be demonstrated in the liver and kidneys. This fact, together with the paucity of megaloblasts in the bone-marrow, indicates that the anæmia was not primary in type. While the hyperactivity of the hæmolymp glands would explain the anæmia which undoubtedly existed before the accidents, the intestinal hemorrhages following them reduced the patient to his state on entering the hospital.

*Pathological Diagnosis.* Dislocation of the spleen with marked elongation and torsion of its vessels, and thrombosis. Chronic passive congestion and fibrosis of the spleen. Interlobular atrophic cirrhosis of the liver. Chronic passive congestion with beginning central cirrhosis of the liver. Chronic passive congestion of rest of portal system. Compensatory hyperplasia of hæmolymp nodes. Hyperplasia of the bone-marrow. Secondary anæmia. Moderate diffuse emphysema of the lungs. Tuberculosis of bronchial and tracheal glands.

My thanks are due to Dr. W. T. Howard, Jr., for the use of material and for his interest in the work.

3. GENERAL SUMMARY. The patient's previous history of pallor, digestive disturbances, and pain in the splenic region, symptoms of which there is a history for a number of years, strongly suggest the

early stage of a splenic anæmia. The frequent urination and the pain in the splenic region also would imply a long-standing dislocation of the spleen. This is corroborated by the enormous elongation of the splenic vessels. Whether or not all the twists in the splenic veins occurred at the time of the two accidents, it is impossible to state, but it is at least more reasonable to suppose that from their multiple character they did not all occur at one time, but that some had existed previously.

The thrombosis of the splenic vessels must have been the cause of the sudden enlargement of the spleen while the patient was in the hospital. The lack of organization in the thrombi of the vessels removed at the splenectomy proves this.

If Banti's stage of splenic anæmia is limited only to those cases in which the cirrhosis is a terminal manifestation we cannot include our case in that category, for the cirrhosis of the liver is certainly of as long standing as the fibrosis in the spleen. We prefer to regard the case as one of splenic anæmia associated with a cirrhosis of the liver, not as a result of the process in the spleen, but rather accompanying it.

The enormous elongation and torsion of the vessels associated with the dislocation of the spleen possess a very probable etiological significance in this case.

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## SARCOMA OF THE SMALL INTESTINE:

WITH EXTENSIVE METASTASIS IN THE HEART MUSCLE AND EMBOLISM OF THE SUPERIOR MESENTERIC ARTERY.<sup>1</sup>

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In 1900 I published five cases of sarcoma of the small intestine and collected about fifty other cases from the literature.<sup>2</sup> Since that time we have had in the hospital ten further cases of this disease, in addition to which a small number of cases has also been reported by various other observers, most of which are collected in the valuable monograph of Lecène<sup>3</sup> published during the past year.

In none of the cases which I have seen or which I collected from the literature was there any note of metastatic deposits in the heart,

<sup>1</sup> Demonstration at the meeting of the New York Pathological Society, December 14, 1904.

<sup>2</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1900, vol. cxx. p. 309.

<sup>3</sup> Les tumeurs malignes primitive de l'intestin grêle, Paris, 1904; Mittheilungen aus den Grenzgebieten, Bd. vii. Heft 415.

and this is the first time we have encountered such marked involvement of the heart in any case of growth.

The patient, a male, aged thirty-five years, was admitted to Mt. Sinai Hospital on July 26, 1904, and died on August 19th. He was under the care of Dr. Gerster, to whom I am indebted for the use of the clinical history.

*Family History.* Presents no points of any importance.

*Previous History.* Four years ago he had an attack of pain in the hypogastrium lasting two days, which was relieved by morphine. He had no chill at this time and no pain in the loins, nor along the course of the ureter. The pains did not radiate; the urine was clear. Three and one-half years ago he had a second similar attack; two years ago he had a third attack lasting five weeks, for the last two weeks of which time he was taken care of in another hospital.

*Present History.* Since the last attack he was well until four months ago, when the hypogastric pain returned, and he developed pains in the left loin, sticking in character. These pains did not radiate downward. For the last two months he has had pain at the end of the penis during urination; the stream is never interrupted and the urine is always clear. He had been getting up once every night for the past three weeks to urinate. Three weeks ago he began to vomit all his food; this lasted one week. He has not been jaundiced. Has been in bed since the vomiting began. He thinks he has lost fifteen pounds in the last year.

*Examination on Admission.* The external lymph nodes are not enlarged, except those in the submaxillary region, which are slightly enlarged.

*Heart.* The dulness extends from the right border of the sternum to the nipple line; the apex-beat is not made out; the sounds are weak; the first apical sound is short, with very little muscular quality. *Pulses* are equal, regular, rapid, of poor force, markedly dicrotic. There is marked sclerosis.

*The lungs* present the signs of emphysema, with slight bronchitis.

*The liver* is enlarged to one and one-half fingers below the free border of the ribs.

*Spleen* not palpable.

*Abdomen* is held rigid, is generally tympanitic; there is marked tenderness just above Poupart's ligament on the left side.

*Genitals* show no changes.

There is no œdema of the legs.

*Rectal Examination.* Prostate negative. Commencing about one and one-half inches above the prostate and extending up beyond the reach of the finger is a mass feeling about as large as an orange, extending somewhat more to the left than to the right, movable, nodular. Pressure exerted upon this causes pain to be felt at the end of the penis. The tumor bulges somewhat into the anterior wall of the rectum.

The patient was operated upon on July 30th by Dr. Gerster. On opening the abdomen, the appendix was found adherent to a large mass filling the true pelvis. The mass itself was found to be a tumor involving the intestines, which would not permit of removal.

From the subsequent history of the case we shall give a few data only:

*August 2d.* Vomiting frequent; temperature 100° to 101°; no pain.

*5th.* Bowels moved; no vomiting since the fifth day after operation. Temperature 101.6°.

*6th.* Flatness over the right lower lobe; breath sounds distant and blowing; crepitant rales.

*8th.* A fecal fistula has developed.

On the 13th large lymph nodes were felt in the left groin. There developed at the base of the left lung dulness and a few mucous rales. The patient died on August 19th.

The urine was usually of specific gravity of 1020 to 1030, contained a trace of albumin, a few red blood cells, pus cells, mucus, and many bacteria.

The autopsy examination was restricted to an examination through the wound.

*Abstract of the Autopsy Report.* *Thymus.* No traces found.

*Esophagus.* Moderately dilated.

*Lungs.* In the left pleura there is a large amount of fluid; in both lungs there are hemorrhagic infarcts and areas of new-growth. The bronchial nodes are enlarged, pigmented, and infiltrated. The posterior mediastinal nodes are also infiltrated.

*Heart.* Weight, 510 g. On the surface of the right ventricle and auricle are several rounded hemispherical prominences, white in color, 2 to 3 cm. in diameter. All the chambers are dilated. The foramen ovale is slightly open. The wall of the right ventricle is thickened. The color is grayish-red, particularly near the septum. There are a few small parietal thrombi. The tricuspid valve is thickened. Left ventricle: The cavity is dilated; the wall is 2 cm. thick, is gray in color, with a slight admixture of red; it is rather friable. There is evidently a very marked diffuse infiltration by new-growth. The mitral valve is thickened; behind one of the papillary muscles is an adherent decolorized thrombus.

The *aorta* and *coronary arteries* show fatty changes.

*Spleen.* Enlarged; marked perisplenitis; a few anæmic infarcts; congestion.

*Liver.* Weight, 1½ kilos. On section congested, cloudy, fatty; a few small areas of diffuse growth in the right lobe near the free border. Gall-bladder: Wall, ½ cm. thick; diffusely infiltrated by new-growth.

*Kidneys.* Several anæmic infarcts in each kidney; also areas of new-growths, which shade gradually into the kidney tissue proper; a few of these are elevated; pelvis dilated; ureters negative.

*Pancreas* and *adrenals* negative.

*Bladder.* There is infiltration by new-growth of the posterior wall up to the mucosa; there are several blackish areas on the posterior wall; the vessels of the trigone are injected.

*Stomach* dilated; wall acutely inflamed.

*Intestine.* In the duodenum there is infiltration of the wall, white in color, for a length of 10 cm. The intestine is dilated at this point. Below this infiltration, between it and the main tumor, there are several places at which the intestine is infiltrated for short distances and is dilated. At a distance of 120 cm. from the beginning of the jejunum there is a very large dilatation of the intestine due to infiltration of its wall by new-growth. This dilatation fills the entire true pelvis. The growth is white in color, soft. The greatest thickness of the wall of the dilated intestine is  $1\frac{1}{2}$  cm. On section the growth is white and soft. The inner surface is necrotic and ulcerated. It is adherent to the bladder, which is infiltrated by contiguity, and is also adherent to the sigmoid flexure and coils of small intestine. It lies above the prostate, not attached to it.

The *mesenteric nodes* are enormously enlarged; on section they are white in color, with yellow areas. The *cæcum* is dilated. The rest of the colon is collapsed.

*Superior Mesentery Artery.* Just above the bifurcation there is an adherent, partially decolorized thrombus which extends slightly into both divisions of the vessels, not entirely filling their lumina.

*Microscopic Examination.* A large amount of material from the case was studied, but only a brief report will be given here. The primary tumor of the intestine proved to be a lymphosarcoma. The lungs, heart, kidneys, spleen, mesenteric nodes, liver, gall-bladder, and urinary bladder wall showed metastases. The pancreas and adrenals showed no metastases. In the wall of the left ventricle and in the septum there was found to be a very extensive infiltration by new-growth, the individual muscle fibres being crowded apart by the cells of the new-growth (see illustration). There was marked degeneration of muscle fibres. The spleen and liver showed marked pigmentation. In the lung there were chronic interstitial changes and small purulent foci. The kidneys and liver showed parenchymatous degeneration. In the intestine the growth was found to begin in the submucosa and to infiltrate between muscle bundles.

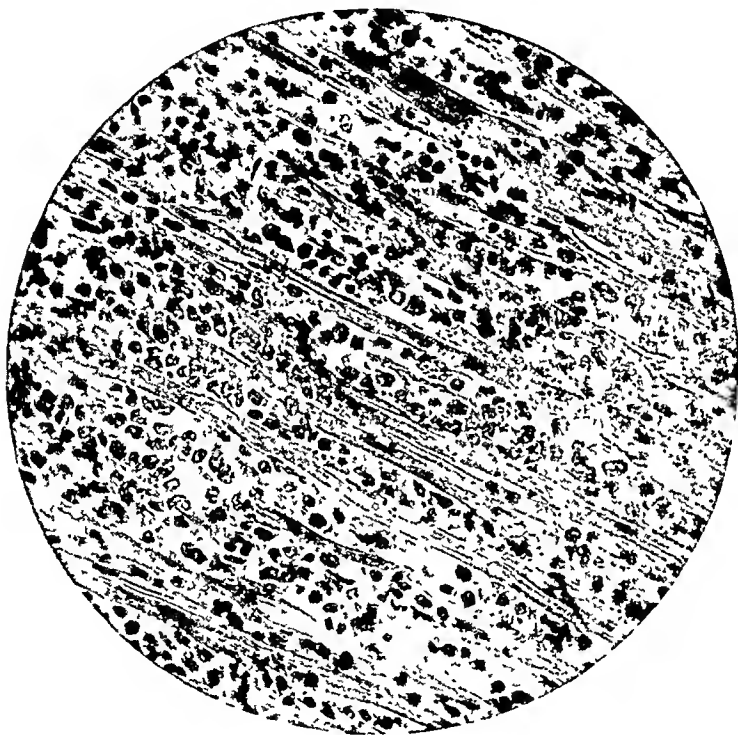
There are several points of interest about this case:

1. It is a very good example of the dilatation which often occurs with lymphosarcoma of the intestine. In this case the dilatation was more marked than any other I have ever seen.

2. As is quite common in these cases, there was no ascites, and no enlargement of the external lymph nodes.

3. The growth in the pelvis with adhesion to the bladder is a characteristic of some of these tumors, which deserves more attention from a clinical standpoint than has heretofore been given it.

4. The duration of the disease is the longest that we have noted in any case. Although from the standpoint of the findings in the case we would ordinarily have diagnosed a lymphosarcoma of the small intestine, the long duration of the case led us to suspect a non-malignant neoplasm or tuberculosis of the intestine with adhesions to the bladder. Baltzer put the duration of the disease at from two weeks to one and three-fourths years, and said that most cases died in nine months. Rutherford described one case with a duration of two and one-half years. In the series of cases which we had collected, this last-mentioned case was the longest one.



5. The embolism of the superior mesenteric artery caused no appreciable phenomena clinically, nor did it cause any change in the intestine. This was probably due to the fact that it was quite recent and that the embolus did not completely close off the lumen of the vessel.

6. The involvement of the heart was the most striking feature of the case. Although a note was made on admission to the hospital that the first heart sound had very little muscular quality, there was no suspicion that the heart was involved by new-growth.

The illustration, for which I am indebted to Dr. Mandlebaum, shows the infiltration in the heart at a magnification of 250 diameters.

THE CLINICAL ASPECTS AND DIFFERENTIAL DIAGNOSIS  
OF APPENDICITIS AND TYPHOID FEVER.

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IN this short paper it is not our intention to give a detailed description of all the clinical manifestations belonging to typhoid fever, or appendicitis, or to the various forms that these two abdominal affections may take on. Our aim is to consider the principal elements of a differential diagnosis rather than to give a long description of the symptomatology; in other words, we have more in view the study of abnormal forms of typhoid fever which may closely simulate appendicitis and thus cause much hesitation on the part of the physician and surgeon. A typhoid fever following its normal and regular evolution without complications only distantly resembles a typical attack of appendicitis, so that it would be difficult to mistake one for the other; but there exist, on the contrary, certain abnormal forms, and they are by no means infrequent, in which considerable difficulty in diagnosis arises. In the first place the mild forms of typhoid should be mentioned. It is well known that in some of these the temperature is not very high, the rose spots may be so discrete that they are usually unnoticed, while the bronchitis may be wanting and the headache very slight. In these cases of mild intensity the diagnosis of typhoid will be based exclusively on a slight pain that may be made manifest by palpation of the right iliac fossa, accompanied by a slight headache and a trifling enlargement of the spleen. Diarrhœa frequently is absent and may even be replaced by constipation. Then again it should be recalled that some of these cases are so slight that the patient does not feel sick enough to remain in bed; in other words, walking typhoid.

The same may be said of cases of attenuated typhoid, which are apyretic and can only be diagnosed by the Widal reaction. All these cases may simulate the commencement of appendicitis where the pain in the right iliac fossa is very slight, while other symptoms indicating a disturbance of the gastrointestinal tract are present to a certain degree, and all surgeons are aware that this form is not exceptional. There are cases of appendicitis commencing by symptoms of enterocolitis, accompanied by a persistent diarrhœa, and, on the other hand, there are instances of appendicitis with a very slow and almost apyretic evolution, commencing insidiously, and where large and extensive plastic exudation, with considerable abdominal distention, easily conceals the purulent focus. Consequently, under these circumstances, an erroneous diagnosis of mild

typhoid is quite possible. And since typhoid fever, even very mild and apyretic, may suddenly become complicated by a superacute perforating peritonitis, just as is met with in cases of insidious appendicitis, it can be readily seen how a diagnosis may be difficult. On the other hand, certain serious types of typhoid may lead to a confusion in the diagnosis just as in the case of the lighter types. I do not intend to refer to the serious forms accompanied by marked nervous or hemorrhagic phenomena, in which the diagnosis falters between meningitis, acute miliary tuberculosis, or any other acute affection other than appendicitis. But there exist certain serious forms, inasmuch as there is an early and intense reaction of the intestine on the peritoneum with a predominance of serious abdominal symptoms, more than by the symptoms furnished by the general condition of the patient. Now it may be stated that for these forms, as well as for others, nothing is more variable than the intensity of the various symptoms of typhoid; abdominal distention, pain in the right iliac fossa, and diarrhoea may reach the maximum point, while the rose-spots may be extremely discrete, hardly any bronchitis, and nervous phenomena practically *nil*. Many authorities appear disposed at the present time to admit that a marked eruption of rose spots is more apt to belong to a typhoid of medium or slight degree; and, on the other hand, it is well known that the rose spots never appear before the seventh or eighth day of the disease. Consequently, when in presence of one of these cases having a predominance of marked abdominal symptoms, a hesitancy in diagnosis between typhoid and appendicitis will be quite possible, at least during the first week of the malady. And *a fortiori* one may be extremely embarrassed in cases presenting a true peritonitis, or one resulting from a perforation. It may be added that it is not rare to meet typhoid with a fever of  $39^{\circ}$  or  $40^{\circ}$  C. during the first twenty-four hours, and these cases with a sudden commencement render the diagnosis a difficult matter.

To sum up, there exist many cases in which typhoid and appendicitis take on similar characters and are extremely difficult to distinguish one from the other, and these usually represent the forms of medium intensity of both these diseases; there are a certain number of symptoms which are common to both, especially pain in the right iliac fossa with or without gurgling on pressure, abdominal distention, a rise in temperature on the very first day of the disease, enterocolitis, and diarrhoea. With these symptoms others may be met with which belong distinctively to each of these affections. The absence of pulmonary symptoms, rigidity of the abdominal muscles, the condition of the pulse, and symptoms of peritonitis would be in favor of a diagnosis of appendicitis when they exist. Bronchitis, severe headache, insomnia, epistaxis, rose spots after the eighth day, and hypertrophy of the spleen point to typhoid fever. We here merely mention the symptoms common to



both diseases, or belonging to them in particular, and will study their semeiological value later on.

From this cursory description it becomes evident that the differential diagnosis between typhoid fever and appendicitis is frequently a very difficult matter. A positive diagnosis of either of them may be difficult in those frequent cases in which several of the cardinal symptoms are wanting. As to the differential diagnosis it is sufficient to review the numerous errors which have been made to convince one's self of the extreme difficulty in which the clinician is frequently placed. Thus, for example, only to point out one of the principal causes of mistake an appendicular colic may be taken for one due to nephrolithiasis, gallstones, intestinal occlusion, or lead colic. Appendicitis has also been mistaken for an acute tuberculous peritonitis, more frequently for a salpingitis or typhoid fever. These cases we will not consider because we only intend to study the differential diagnosis of appendicitis in general, and we will limit ourselves to the differential diagnosis with typhoid fever. In a case reported by Bayet, the patient was a young woman who was suddenly taken with febrile phenomena, accompanied by a slight indefinitely localized pain in the right iliac fossa. On account of the large size of the right tube, a diagnosis of acute catarrhal salpingitis was made, and this diagnosis appeared all the more justified because, under the influence of quiet and appropriate treatment of this slight local lesion, the temperature fell in two or three days. The patient appeared to be cured when she was suddenly seized by an acute pain at McBurney's point with serious general symptoms and a high temperature. As the diagnosis of appendicitis did not appear to be a matter of doubt, the patient was operated on the next day. The appendix removed was of normal size, slightly hyperæmic, and contained a clot of blood, an important fact to which we will return later on. In spite of the operation the disease became worse and the patient died a few days afterward. Autopsy showed characteristic ulcerations of typhoid fever. The night before death Widal's test was positive.

Several other similar cases have been published, and a number of authorities have only mentioned the possibility of a mistake in differential diagnosis, without going into any details.

We must not lose sight, in the appreciation of the elements of the differential diagnosis, that appendicitis is a disease that must be recognized at its very beginning. Upon the precociousness of this diagnosis depends the indications for operation and the patient's life; consequently, when one is in the presence of one of these difficult cases that we have already considered, and when one hesitates between an abnormal form of typhoid fever and appendicitis, too much precaution cannot be taken in making the diagnosis, and this diagnosis should be based on the greatest number of

elements possible. These elements of differential diagnosis may be classified under four heads, as follows:

(1) An analysis of the clinical symptoms; (2) examination of the urine; (3) examination of the blood; (4) Widal's serodiagnosis.

The clinical symptoms leading to a differential diagnosis are essentially variable, and no one, taken alone, is pathognomonic. Consequently, one should take into consideration the ensemble of these symptoms rather than any one of them; and in spite of such grouping, the clinical aspect of the disease is, under certain circumstances, absolutely insufficient, and, in order to come to any conclusion, one should take into consideration the ensemble of the other symptoms, to which we will refer later on.

It is, however, often possible to obtain considerable information from an attentive study of the case, which will allow of making a serious presumption, if not a certitude of the diagnosis. Among the symptoms common to the two diseases, pain in the right iliac fossa is the most constant, but its value is not an absolute one and is not sufficient to enlighten the diagnosis. It is true that this pain, in cases of appendicitis, is more apt to be sudden and to merit the name of appendicular colic, while the pain of typhoid is more inclined to be insidious in its evolution, shooting and not pungent, as in appendicitis. Taking into consideration that in the majority of cases spontaneous pain is less frequent and less acute in typhoid, that palpation of the abdomen gives rise to sudden and exquisite pain in appendicitis, and that the localization of this pain is different in each affection, one may draw some conclusive evidence in favor of one or the other. In typhoid it is spread out through the entire iliac fossa, while in appendicitis it is quite limited, and in many cases is particularly intense over McBurney's point. Now, although this is true in a large number of cases, the characters of the iliac pain present numerous variations, and the differences that we have pointed out are subject to many exceptions, which may lead a physician into error if he is not on his guard.

In the first place the pain in the right iliac fossa may be absolutely wanting, or very attenuated and temporary, both in certain forms of typhoid fever as well as in some cases of appendicitis. It is well known that the symptomatic pain is very variable in appendicitis, not only in its acuity, but also in its localization, and a certain number of cases have been reported where its greatest intensity was found in the left iliac region. In quite a few cases the greatest point of pain will be found either above or below McBurney's point. Then again pain in the right iliac region may be induced by other entirely different affections, such as a calculus or a salpingitis.

With the pain we should also mention intestinal gurgling on palpation of the iliac fossa, but only for the purpose of eliminating it as a diagnostic sign. It has absolutely no value, and simply indicates the presence of gas in the intestine.

Muscular rigidity, on the contrary, was for a long time considered as a most important symptom, always speaking in favor of appendicitis, particularly when the process had gone on to suppuration. At the present time it is impossible to retain the importance that was formerly given to this symptom, because if one palpates an iliac fossa, containing some lesion, pain nearly always will be produced, immediately followed by a reflex contraction of the abdominal wall, which instinctively puts itself on the defence. Now, one can readily imagine that the pathogenesis of the symptom of muscular rigidity is a very general phenomenon. When the distention is not very pronounced in a case of typhoid, palpation may produce a contraction of the abdominal walls, and, on the other hand, in some cases of clinically characteristic appendicitis, verified pathologically, this symptom may be very slightly marked, or even be absolutely wanting. Consequently, it may be said that the absence of muscular rigidity, which is ordinarily the case in typhoid, may also exist in appendicitis, and the semeiological value of this symptom is only relative.

Cutaneous hyperæsthesia has not much value.

We do not believe that there is any more certitude in the temperature curve, the height of the fever in the commencement, and the symptoms of enterocolitis, because in subacute or chronic appendicitis the temperature chart looks very much like one of typhoid, and even if there existed very distinct differences in this respect, this symptom would only have a relative value in the question we are now considering, because it only begins with the commencement of the disease. I have already said that there are cases of appendicitis without fever just as there are cases of apyretic typhoid.

The best guide, when they are present at the commencement, are the symptoms of enterocolitis. In many cases appendicitis is accompanied by constipation at the onset, but to this rule there are numerous exceptions, and diarrhoea may be quite as persistent and as abundant as in typhoid. Inversely it is not infrequent to meet with cases of typhoid in which diarrhoea is absent and is replaced by constipation during the greater part, if not the entire duration, of the disease. As to vomiting it is observed at the onset of typhoid as well as in appendicitis, and gives no clue to the diagnosis.

From all this it goes to show that the clinical symptoms common to both diseases may be present in either one or the other, presenting very similar characters which will prevent one from utilizing them in making a differential diagnosis. When the typhoid presents no other symptoms, it will be clinically impossible to diagnose it, but it is only right to say that in practice such cases are not often met with. In typhoid from the very beginning the headache is extremely severe, and an important character is that it becomes better as time goes on and the abdominal symptoms increase in intensity. In appendicitis headache is practically absent, and when it does exist

it does not follow this same progressive diminution. Bronchitis is also wanting in appendicitis, but it also is not at all marked during the first few days of typhoid. The epistaxis, when it occurs at the beginning of typhoid, is more valuable, but insomnia during the first few days appears to have, in our way of thinking, a still greater importance; associated with an intense headache it certainly pleads greatly in favor of the latter affection. The appearance of a marked eruption of rose spots is a certain sign of typhoid, but, unfortunately, this does not occur before the seventh or eighth day of the disease, and I have already pointed out the necessity attached to an early differential diagnosis. It should be remembered that in a number of cases the rose spots may be absent, either really so, or they are so discrete and ephemeral that they pass by unnoticed. Hypertrophy of the spleen is possessed of no pathognomonic value and simply indicates the degree of the infectious condition of the patient, and it is well known that certain cases of appendicitis take on the characters of hypertoxic infectious diseases. A rapid pulse, prostration associated or not with a variable degree of delirium, like a pinched expression of the face, may be observed in many cases of serious infection, as in typhoid.

It would appear to result from the above considerations that no single symptom taken in itself is possessed of a pathognomonic value, but it is not at all doubtful that when taken altogether these symptoms give a positive diagnostic indication, infinitely more precise than the analysis of any one of these symptoms taken singly. And there exist a certain number of cases in which, by reasoning, a diagnosis may be made with only a small chance of making a mistake. But, on the other hand, there are other patients in which the affection assumes such an aspect that it is absolutely impossible to determine its nature with certitude, and these are those instances where the symptoms appear to multiply themselves to such an extent that the physician is absolutely lost. The localization of the pain, exactly on MacBurney's point, the sudden and dramatic commencement, accompanied by high fever, vomiting, hiccough, in a word all the symptoms of a very acute appendicitis, have been observed with the greatest distinctness to such a point that an operation has been decided upon and immediately done, when in reality the case was one of typhoid, the patient possessing a perfectly normal appendix. Cases of this description defy all analysis, but fortunately there are others in which the study of the symptoms in their ensemble makes a less difficult interpretation. In point of fact, in the majority of cases the abdominal symptoms are those which are foremost in the clinical picture of typhoid, while, on the contrary, the gravity of the general condition often overshadows from the very commencement all other signs found upon local examination, when the case is one of appendicitis. Without making this an absolute rule and without forgetting those cases of typhoid,

happily infrequent, in which from the very start the general symptoms become alarming, it is nevertheless quite permissible to suppose that we have here a serious element for appreciation in the diagnosis; given an equal gravity, an appendicitis manifests itself by more accentuated general symptoms than a typhoid, especially during the first week, and the abdominal symptoms are, on the contrary, less marked in the latter than in the former.

The commencement of the symptoms, their manner of acting in the beginning, should also to a certain extent be taken into serious consideration. Generally speaking, the commencement of a typhoid fever is insidious and the temperature curve is progressively ascending; while usually in acute appendicitis, on the contrary, the commencement is sudden and the fever high from the start. However, we know that this rule has many exceptions. The evolution of the symptoms may also, under certain circumstances, help in the diagnosis. Typhoid has usually a regular and cyclical evolution, while that of appendicitis is capricious, often proceeding by successive steps and subject to recurrence. However this may be, it is clearly evident that the clinical symptoms taken singly, or considered in their ensemble, have occasionally only a very relative semeiological value, and their analysis in certain cases only gives a more or less serious presumption in favor of one or the other of these two diseases. In some exceptional cases the symptoms, although very rationally interpreted, will be in absolute disaccord with the true diagnosis.

The examination of the urine, which is absolutely necessary in all cases, even the simplest, has a still greater importance when the case is a doubtful one. In all acute febrile diseases albuminuria is usually present and consequently may be met with both in typhoid and in appendicitis. However, if one will observe that at the time the first symptoms appear appendicitis is a local affection, while, on the other hand, the first positive symptoms of a typhoid indicate a diffusion already realized of the typhoid toxins throughout the entire economy, it would seem probable that, in the beginning, at least, albuminuria will be more frequent and more pronounced in typhoid than in appendicitis. In the former the kidney is already under the influence of the toxin, while in the latter the toxin has not as yet had time to be produced. Now this remark, which may at first sight appear somewhat theoretical, is fully confirmed clinically. It is with intent that we insist upon the fact that we are referring to the commencement and later, when the appendicular lesions have allowed the toxins to become diffused throughout the economy on account of the close pocket in which they are manufactured, susceptible of completely destroying organs such as the liver, and which can result in death with all the symptoms of a hyperacute poisoning, large quantities of albumin will be found in the urine.

Indicanuria is of an absolutely secondary diagnostic value, because indican may be found in the urine in all infectious conditions of the digestive tract and an ordinary attack of indigestion is quite sufficient to make it appear. According to a certain number of authors indicanuria is never absent in typhoid, but others have upheld that it is absent in the commencement and its maximum reached during convalescence. On the other hand, a large quantity of indican may be found in the urine during the first few days of appendicular infection, and, consequently, this is a differential symptom which may, to a certain extent, be utilized; but I would repeat that, according to my way of thinking, its importance is only secondary. Certain indications may also be derived from the toxicity of the urine, and this has been especially studied in children during appendicitis by Lannelongue and Gaillard. From their researches it becomes evident that in appendicitis the urinary toxicity increases at once, at the same time that the density increases and its color becomes dark. On the contrary, in typhoid, the toxicity becomes above the normal, principally at the beginning of convalescence at the time when the patient is undergoing a urotoxic crisis, which becomes manifest by a considerable increase in the quantity of urine, corresponding to a discharge of extractive substances from the organism.

Blood examination may give in many cases valuable hints and the importance of hæmatology in the study of these diseases is greatly appreciated at the present time. I do not believe that it is too much to say that the recent method devised by Ehrlich, in allowing one to classify the various forms of leukocytes, not only according to their forms in general and their nuclei, but according to their affinity for basic or neutral coloring acids, has given a new impulse to the histology of the blood and has completed the study of the characters that this tissue presents in infections and intoxications. But it must be admitted that this study, which for the various leukæmias is still incomplete, has just been begun in the greater number of other affections. It is far from our intention to make a detailed study of the condition of the blood in appendicitis and typhoid, and we will only refer to certain characters which may aid in making a differential diagnosis. In appendicitis the clot is found microscopically to be composed of an abundant fibrinous network, and this aspect, which is found in all inflammatory diseases, does not exist in septic affections like typhoid; this characteristic may consequently be utilized in a certain number of cases. However, on the very account of its generality, one can readily see that it can only be utilized in certain cases where the differential diagnosis is faltering between the two diseases which we are considering. It consequently will be absent in certain forms of appendicitis which very rapidly take on the aspect of septicæmia, or in some instances of typhoid complicated by inflammatory accidents

and commencing with them, as, for example, pneumotyphoid or pleurotyphoid. The examination of the serum does not give any marked result, but sometimes in typhoid the clot is small and the serum proportionately abundant; occasionally also in certain hemorrhagic forms of this disease the serum takes on a hæmoglobinuric color, but these are characters far too inconstant to take seriously into consideration.

The study and the numbers of the figured elements have a much greater importance, and it is known that in inflammatory infections, like appendicitis, especially when it is of the suppurating variety, the number of leukocytes increases very greatly. On the contrary, in typhoid fever and septic diseases, without inflammatory complications, the count remains normal; and there may even be a hypoleukocytosis. This sign accompanied by an absence of the fibrinous exudate takes on a very great diagnostic value which has been pointed out by Hayem: "In cases of typhoid without any inflammatory complication he points out it is a characteristic of the disease; the absence of a fibrinous reticulum and the small number of leukocytes visible in the field of the microscope." (Lenoble.) Muehleck has also found a diminution in the number of red cells, as well as their value in hæmoglobin in many cases of typhoid fever. To sum up, it may be said that an examination of the blood should never be neglected in doubtful cases; unless there are inflammatory complications in typhoid, or a hyperacute septicæmia of appendicular origin, it will often give very useful indications for the differential diagnosis of these two affections.

Of all the means of investigation at our disposal the serodiagnosis of Widal is assuredly the one that gives the most certain results other than the clinical symptoms. In all doubtful cases of typhoid fever the research for this sign has a capital importance and in itself alone it will allow one to distinguish a mild typhoid from slight gastric disturbance, a serious typhoid from a meningitis, or all other affections which may simulate it. In many cases where there is any hesitancy in the diagnosis between a typhoid and an abnormal appendicitis the serodiagnosis will settle the question, and where the result is positive this sign has absolute certainty. However, without wishing to decrease the great value of this reaction, it is necessary to bear in mind that it is occasionally absent under certain circumstances, and it is precisely these that must be looked for, particularly in those cases where the diagnosis of appendicitis is faltering.

In the first place there are some few subjects whose serum does not agglutinate, or only very slightly so, the culture of Eberth's bacillus, although they are manifestly the possessors of typhoid. Such cases are reported from time to time, but they are generally speaking exceptional. As a rule, the seroreaction does not become manifest before the seventh or eighth day of the disease, and it

cannot be too often repeated that when there is any confusion with appendicitis it is at the commencement of the affection that the problem must be solved; to wait a week before deciding to operate would cost many lives. It consequently becomes evident that, in the particular case which we are considering, the importance of Widal's test is much less and this sign will practically lose all its value when it appears late in the affection.

It is not at all infrequent to meet with tardy agglutination, only appearing a fortnight or eighteen days after the commencement of the typhoid, and in these cases the time at which the serum test becomes positive naturally takes away the greater part of its importance. On the other hand, it would seem from the most recent works on the subject that agglutination is all the more apparent the more the typhoid retains a medium intensity and a normal evolution. In serious typhoids the agglutinating reaction is often *nil* or hardly marked, which is another circumstance calculated to cause a diagnostic error. In point of fact it is known that the patient's serum, under the influence of typhoid infection, having acquired the property of agglutinating typhoid cultures, will retain this property for a considerable length of time after recovery from the disease, and this agglutinating property may show itself a year, or even more, after typhoid. Now, as an appendicitis may develop consecutively upon a typhoid after a more or less long lapse of time, it is easily conceived that before rejecting the diagnosis of appendicitis in cases where the serum test is positive, one should always obtain a history of the morbid antecedents of the patient, and with this reserve Widal's test possesses a diagnostic value of the highest order and one that should never be neglected in doubtful cases.

In the preceding pages we endeavored to ascertain upon what elements a differential diagnosis between typhoid and appendicitis might be made, and we will now endeavor to apply what we have learned to certain cases which may be met with clinically. We will limit ourselves to the principal ones, voluntarily leaving aside the very numerous intermediary types whose description would extend the subject matter of this paper without profit.

One may find himself in the presence of a slight infection, characterized by a gastroenteritis of medium intensity with headache, moderate fever, and pain in the right iliac fossa. Under these circumstances the development of the disease can only rarely help the clinician to decide upon the diagnosis which may very well be faltering between a mild typhoid fever in the beginning, a simple gastrointestinal intoxication, or an attenuated appendicular colic. Muscular rigidity and cutaneous hyperæsthesia are usually wanting and the localization of the pain will be difficult. Given such a symptom-complex, the degree and progress of the headache, insomnia, if the disease is at its commencement, the appearance of



rose spots and serodiagnosis, if the disease has attained the end of the first week, will be, according to our way of thinking, the principal signs upon which one may base the diagnosis.

Under other circumstances, a physician may be called to a patient presenting all evidences of a serious disease and in which the predominating symptoms will be abdominal. The case will not look like one of true peritonitis, but the abdomen will be distended with acute pain in the right iliac fossa and either a profuse diarrhoea or an obstinate constipation will be present. Under these circumstances the development of the symptoms is valuable and will be completed by the elements furnished by clinical examination, as well as by the examination of the blood and urine, as we have already pointed out, and if Widal's sign is positive the diagnosis becomes evident. In other cases one will find a confirmed peritonitis, in which case the pathogenesis and etiology must be ascertained. Formerly two distinct types of acute peritonitis, occurring suddenly during a febrile malady were distinguished; one group was called peritonitis by propagation, the other from perforation, and to each of these modalities was connected a special clinical invasion. At the present time it is known that a large number of the so-called peritonitis cases from propagation are due to perforation, although the latter may be extremely minute, but existing nevertheless, and it may be said that the form by propagation is very infrequent, if in reality such cases really exist.

Let us suppose that the case presents the ordinary symptoms of a perforating peritonitis, the question will at once arise as to whether it is due to a ruptured appendix or a perforated typhoid ulcer. This is occasionally a very delicate matter to determine, all the more so because in other diseases, in gastric ulcer, for example, the same condition may arise. But the difficulty is quite great enough for us to limit ourselves to the consideration of the two diseases which we are studying. In some cases the differential diagnosis will be quite possible if the age of the disease is considered, because a perforation of a typhoid ulcer infrequently takes place before the second week and rarely occurs after the third. Generally speaking, perforation of the appendix is much more precocious and may even take place during the first few hours after the development of the symptoms, and the disease may at once show itself with all clinical characters of perforation. In doubtful cases the initial localization of the pain should be carefully ascertained, as well as the condition of the spleen and lungs; one should watch for the possible appearance of rose spots, as well as the existence of a leukocytosis and the presence or absence of Widal's sign in those cases where the disease has lasted for a week or more. The time at which the perforation occurs, and the preceding evolution of the disease, as well as the serodiagnosis, will, we believe, serve as the principal diagnostic elements in these cases

which rapidly take on the role of toxæmias more than inflammatory processes.

A typhoid complicated by perforation rarely gives rise to a circumscribed peritonitis, and usually one will be dealing with a diffuse inflammation of the peritoneum, while a localized peritonitis is more frequently observed in perforation of the appendix. Cases of periappendicular abscess are rarely mistaken for typhoid, because they are easily diagnosed by the muscular rigidity which, under these circumstances, is rarely wanting, as well as by the temperature chart, the small, rapid pulse, and other signs of intra-abdominal suppuration. If there is any doubt, examination of the blood and urine will have no very great importance, because, in these inflammatory processes, with a tendency to suppuration, leukocytosis will almost always be present, whether the case is one of suppurating appendicitis or a typhoid complicated by some inflammatory lesion. Consequently, it is well to base one's self more upon the elements furnished by the clinical evolution of the disease and to the Widal test.

So far we have compared appendicitis and typhoid fever, but we should now consider those cases where both diseases simultaneously exist in the same patient; in other words, can an appendicitis complicate typhoid fever? The reality of this pathological association is not doubtful, although the frequency is a much discussed point. A certain number of authorities are of the opinion that the appendix is almost always involved in typhoid, but that the lesions found are those of slight inflammatory nature not sufficiently marked to give rise to symptoms of a true appendicitis. On the other hand, there are others who classify the cases under two separate heads, namely, those in which the congestion of the appendix remains moderate, and, secondly, those in which a true appendicitis arises during the progress of the typhoid. It is quite permissible to admit that these instances, at the present time well established, cannot be extremely infrequent, and they are, for that matter, possessed of a very rational interpretation. In the first place the lymphatics of the cæcum and appendix are in free communication with those of the end of the ileum, and thus a direct extension of the lesions may take place. But besides this the histological structure of the appendix is in every way comparable to that of the small intestine, and in particular a large amount of lymphoid tissue is to be found which, at certain parts of the organ, may form miniature Peyer's patches. It would, consequently, seem quite natural that this lymphoid tissue can be the seat of an intense hyperæmia, and even go as far as an ulcerative process when Peyer's patches present marked lesions. Now, it is well known that epidemics of appendicitis very frequently coincide with epidemics of general infectious diseases, and many authorities have pointed out the great frequency of appendicitis during epidemics of la grippe, while others have given a general infectious origin to appendicitis.

Among the general diseases it is quite natural to suppose that typhoid should enter for a large share, and in point of fact it can be shown that certain typhoids become complicated, principally during the acute period, by accidents having a distinct appendicular origin. In other cases the appendicitis arises during the decrease of the disease, or during convalescence, and these are the instances that Dieulafoy has described under the appropriate term of paratyphoid appendicitis. The patient hardly recovers from the acute symptoms of the typhoid, he has hardly entered into convalescence, when suddenly characteristic signs of acute appendicitis appear. Lastly, it is not infrequent to meet with appendicitis in patients who have had typhoid one or more years previously.

It now remains for us to examine the mechanism of appendicular accidents occurring in typhoid. Generally speaking this mechanism is little known. In mild cases, where the lesion of the appendix is indistinct, most authorities believe that the symptoms observed are referable to a mere congestion of the organ. This inflammation arises from direct propagation, or by lymphatic propagation, but the process does not go as far as ulceration, and clinically speaking there is not appendicitis. In two cases of typhoid fever during convalescence I have removed the appendix, believing from the symptoms that the organ was the seat of an inflammatory process, and, although macroscopically the organ appeared normal, yet, upon section, its cavity contained a clot, due without any doubt to a hemorrhage arising in Peyer's patches, which microscopically showed evidences of ulceration and which, in all probability, would have resulted in perforation of the organ had the process continued. It may be that the clot, playing the part of a foreign body, gave rise to the symptoms of appendicitis in these patients, but I feel, nevertheless, that at least in these two instances the appendix was better in a bottle than in the patient's abdomen.

As to the question of treatment much could be said, but I shall limit myself to the conduct to be followed in cases where the diagnosis, in the first place uncertain, may be made a sufficient probability of either appendicitis or typhoid, as well as those cases where uncertainty still remains after a careful examination of the various diagnostic elements that we have considered. The rules which should guide the practitioner may, according to our way of thinking, be laid down somewhat as follows: In the first place we will suppose that the diagnosis falters, but only as far as typhoid fever and appendicitis are concerned, and that nothing in the evolution of the disease would lead one to suspect a pathological association of the two processes. Under these circumstances the plan to follow is generally a simple matter. The clinical evolution should be carefully studied and one should surround one's self with all guarantees which are accessorially furnished by the blood, urine, and Widal's test. If the diagnosis inclines in favor of typhoid,

operative interference should naturally be deferred, at least until new symptoms appear which change the first diagnosis. If, on the contrary, the case is one of appendicitis, although one may still have some slight doubt, operation should be at once proposed in order to avoid the always menacing possibility of irremediable accidents, because it too often happens that the surgeon is called too late, but one can never intervene prematurely. However, it may happen that the case is a particularly difficult one, in which all the appearances are in favor of appendicitis, when in reality one is dealing with typhoid. Now, in this case, what will occur if laparotomy is done and the diagnostic error found after the abdomen is opened? Assuredly the operative shock, the narcosis, the pain, and all the ordinary consequences of such an interference are not to be desired in a typhoid infection, but a number of published cases would lead me to suppose that the prognosis is not bad, because the general condition of the patient has not appeared to be greatly aggravated by the operation.

There now remain those cases where during the progress of a typhoid symptoms of appendicitis make their appearance. The course to follow under these circumstances is subject to much discussion, and without considering all that has been said upon it we will simply consider two phases of the question which, according to our way of thinking, are most dissimilar. In the first case we have typhoid symptoms dominating the scene, while those arising from the inflammatory process in the appendix are, or appear to be, of secondary importance. It is possible, as I have already pointed out, that in these cases the appendix is the seat of only a temporary hyperæmia, which, as is known, is not an infrequent occurrence during typhoid. Here the prognosis is relatively favorable and an operation will probably not be necessary. But when the appendicular symptoms take on an intensity capable of leading one to suspect an ulcerative process in the appendix, or when the symptoms of appendicular reaction, in the first place slight, become aggravated, operation is indicated without delay. In closing, I think I can sum up in a word all that has been said in this paper, namely, that every time an appendicitis exists, either alone or associated with typhoid, an operation is indicated. Interference is contraindicated only in cases of simple typhoid, or one associated with symptoms arising from the appendix, but which are so slight that they cannot be considered as due to a true case of appendicitis.

THE LAW AND THE DOCTOR.<sup>1</sup>

BY C. STUART PATTERSON, ESQ.,

OF PHILADELPHIA.

I HAVE selected as the subject of my remarks this evening, "The Law and the Doctor." Under that title I shall, in general terms, discuss the various relations with the law into which the doctor is brought by reason of his profession and his practice; but I shall not attempt the impossible task of providing you with a guide to take you safely through all the mazes and the intricacies of the law.

Under our complicated form of government there are, as you know, laws of the United States, laws of the several States, and municipal regulations of the cities and towns. With the laws of the United States you have, as practising physicians, nothing to do, unless you become medical officers of the army or navy, or Immigration and Quarantine Physicians, or Examining Surgeons under the Pension Bureau; or unless you should reside and practice in the District of Columbia, or in some other Territory directly governed by the laws of Congress. It may, however, be, under the restless activity which now dominates the government at Washington, and under the modern latitude of constitutional interpretation, that it may hereafter be determined to be interstate commerce for a doctor in Philadelphia to send a prescription to a patient in Camden, or for a patient in Wilmington to be brought to a Philadelphia Hospital for operation; or it may be determined that there ought to be one uniform regulation equally affecting medical practice in every part of the United States. Such a conclusion would not be more revolutionary than some that are now discussed. That determination has not yet been made, and doctors will probably not be brought under Federal regulation and control until after the government of the United States has succeeded in fixing the prices at which all commodities are to be sold, and in prescribing the minimum number of children permissible to any well-regulated family. The laws, therefore, which now concern you are the statute law and the common law of the State, and the police regulations of the district, city, or town, in which you may open your office and practise.

At the outset there are to be considered the legal restrictions upon the right to practice your profession. That right has been in England a subject of legal control ever since the third year of the reign of Henry VIII., but in this country the restrictions are of recent origin and development. It is obviously one of the duties of the government to protect its citizens as far as possible against incompetent practitioners, but because of the essential inadequacy of all

<sup>1</sup> An address delivered before the Academy of Jefferson Medical College, April 14, 1905.

human methods of testing competency, otherwise than by actual experience in practice, all that the State can do is to establish certain prerequisites, which, when complied with, shall afford a reasonable probability that the practitioner has undergone a certain minimum of preliminary training. The statutes of each State must, of course, be looked to for a full and accurate statement of the prerequisites required by that State. Speaking generally, the statutes require satisfactory proof that the applicant has attained the age of twenty-one years, is of good moral character, has a diploma from a medical school of recognized standing, given him after attendance upon a course of specified length, has passed a satisfactory examination before a State Board of Examiners, and has filed in a public office the official certificate of his compliance with these prerequisites. These statutes generally except from their operation non-resident consultants, and practitioners not maintaining offices within their boundaries. The statutes impose, as penalties for their violation, in some cases, a forfeiture of professional compensation, and, in other cases, fine and imprisonment.

Pennsylvania and some other States require the applicant to have obtained a competent common-school education. I am glad to know that Jefferson Medical College has, in its requirements for admission to study, gone farther than the statute, and imposed the conditions of either a satisfactory degree or diploma in the arts, or a certificate of successful examination by competent examiners in subjects of greater scope than those of a common-school education.

While it is desirable that everyone who enters upon the study of either law or medicine should, where his individual circumstances are favorable, bring to that study the broadening and the liberalizing influences of residence and training in a great university, and should have that academic degree which is the proof of his opportunities for general culture, it yet is not expedient that the law should make the possession of such a degree a prerequisite to the practice of a learned profession. To do so would be to close the doors of the profession to all save those whom the accidents of fortune permit to indulge themselves in the luxury of college life, and to postpone the time at which they become self-supporting. Under modern conditions of competition and specialization that time is, even if circumstances be favorable, so long deferred, that it is not wise to increase it by a hard-and-fast rule, whose unbending application will not only work great hardship in individual cases, but will possibly deprive the profession and the community of the services of some men of eminent natural ability.

The young doctor of to-day comes to the practice of his profession more generally and more thoroughly instructed than his predecessor of fifty or even twenty years ago. The study of medicine is, because of its technical terminology and because of the complexity of the human body, the most difficult of all professional studies. The

medical course has wisely been lengthened in time and broadened in scope. Yet, bearing in mind the true definition of education as a method of mental development and training, and not as a means of acquisition of information, it may be questioned whether there is or is not to-day a tendency in medical instruction to require of the student, in his days of pupilage, the study of too many topics and the attempt to master too many details. The danger in that is the making of smatterers, whereas the maxim of all educators should be "*non multa sed multum*." Be that as it may, the learned professors in our great colleges, who are training the doctors of the future, may be trusted to check that tendency whenever it becomes certain that it produces undesirable results.

The statutes now in force deal, in general, with the practice of medicine and surgery. That means, strictly construed, the professional treatment of disease by diagnosis, advice as to diet and manner of life, the administration of drugs, and surgical operative interference. Whether the practitioner serves his patient gratuitously or charges for his services does not affect the application of the statutes. Nor, so long as the doctor uses physical means, is it material that he or she is a regular physician or is of the homœopathic or the eclectic schools, or only practices midwifery, or is a bone-setter, or is exclusively a devotee of Dr. Lorenz's methods. All are alike subject to the statutes. But there is a question whether those dangerous modern charlatans, the practitioners of treatment by faith, or of so-called Christian science, are or are not within the statutes. As to this the authorities differ. It has been held, on the one hand, that their non-use of physical means of treatment takes them out of the statute. It has been held, on the other hand, and with greater reason, that, as they do undertake to treat disease, though only by advice and by mental influence, they do practice medicine, and they do bring themselves within the statutes. It is to be hoped, in the interest of the community, that this view will ultimately prevail, and that all professional practitioners of the healing arts will be brought under the statutes, for, undoubtedly, lives have been lost which would have been saved if proper medical treatment had not been prevented by the teachings of ignorance.

The relation between the doctor and his patient is, in the highest degree, confidential. It is necessary for the professional adviser to know all that he can observe, and all that the patient can tell him, as to the cause and nature of the patient's condition, and it is essential to the patient's freedom of communication that he should feel assured that the doctor will regard as confidential all that he sees and hears. The members of the profession have always observed this honorable obligation of secrecy; but the law has not, until recently, permitted the doctor, when called as a witness, to refuse to violate the confidence reposed in him by his patient. Now, in many jurisdictions, the statute declares that "a person duly author-

ized to practice physic or surgery shall not be allowed to disclose any information which he acquired in attending a patient in a professional capacity, and which was necessary to enable him to act in that capacity." In some jurisdictions the protection is limited to other than criminal proceedings. In other jurisdictions, notably in Pennsylvania, the privilege is further limited to that "which shall tend to blacken the character of the patient." In no jurisdiction does the privilege protect consultations for the purpose of committing an act forbidden by law. In all jurisdictions, as the privilege is intended for the protection of the patient, he may waive the privilege, and, if he does so, the doctor may and must testify fully. It ought in all jurisdictions to be determined that the privilege cannot be asserted in lunacy proceedings, or in cases involving testamentary capacity, for otherwise the ends of justice might be defeated. It would be wise for the members of the profession to consider this subject and to endeavor to have the law so amended that the privilege, while more fully protecting the interests of the patient, will not in any way prevent the furtherance of justice.

The doctor is next brought into contact with the law by various regulations of police, which more or less directly affect him in his practice. For the terms and effect of and the results of disobedience to those regulations, the statutes or ordinances, putting them in force should be carefully examined. The most important of those regulations require reports to public officers of births, cases of contagious disease, and deaths, and causes of death, and regulate the distribution of the unclaimed bodies of the dead for dissection, demonstration, and study. There are also in some jurisdictions regulations as to the prescription and administration of poisons, narcotics, and dangerous stimulants. There are also, in many jurisdictions, other sanitary regulations as to which it is well for all practitioners to accurately inform themselves.

The interests of the medical profession and those interests of the community which are inseparably bound to the interests of the profession have not been, as yet, injuriously affected by governmental regulation.

There are, however, tendencies which may in the future produce undesirable results. There are in every community busybodies, who, without adequate knowledge or training, stimulate popular agitation upon technical subjects. The modern agencies of communication, the railroad, the frequent mails, the telegraph, the telephone, and the sensational newspaper, have rendered it easy to manufacture upon any subject an apparent force of public opinion, which is really nothing more than the consolidation of the ignorance and the prejudices of the uninformed, and which, nevertheless, can, and often does, effect hasty and ill-considered legislation. When unwise governmental action is threatened, it can only be met by professional organization and by a campaign of education.



The nature and the extent of the doctor's duty to his patient may be brought into discussion in legal proceedings, either where a patient becomes dissatisfied with the results of his treatment, and brings an action to recover damages for that which he alleges to have been malpractice; or where a doctor, having sued to recover his professional compensation, is met with the defence that the treatment was unskilful.

A doctor may, if he is sufficiently foolish, expressly guarantee his patient's restoration to health, or, in other words, constitute himself an insurer of the success of his treatment; but only quacks and charlatans assume any such obligation. In the absence of an express contract, the implied obligation of the doctor is that he will perform that duty of care for his patient which the law defines and requires.

It matters not whether the services are rendered gratuitously or are properly compensated, for the confidence induced by the undertaking is an adequate consideration for the implied obligation. The standard of that care is and ought to be high. The law, therefore, requires the doctor to exercise with regard to his patient, not only that degree of care which a man of ordinary prudence would exercise under the circumstances, but also that higher degree of care which ought to be exercised by a man who represents himself to be skilled in his calling, and who has assumed to do that whose right performance requires special knowledge and skill.

The doctor's lack of that knowledge, care, and skill is, if injury to his patient results therefrom, actionable negligence on his part.

A surgical operation and a physical examination involving any contact with the person are equally in law regarded as assaults, and it, therefore, is advisable that the operating surgeon or examining physician should, before the operation or examination, obtain the assent of the subject, and, if the subject be a minor of tender years, also of his or her parent or guardian. An assent to a specified operation gives no warrant for another and different operation.

Neither a husband, a parent, or a guardian can be permitted to deprive of the benefit of needed treatment a wife or a child who is of an age sufficient to give consent. While it is not legally necessary in the case of a wife or a child of such age that the consent of the husband, parent, or guardian be obtained, it is, nevertheless, wise for the doctor to secure it.

If an examination involves an exposure of the person, though without physical contact, it is advisable to obtain the like assent.

It must be borne in mind that if the operation be one which a surgeon of ordinary prudence would not undertake to perform, the assent of the patient will not constitute a defence to the surgeon, if he be sued for malpractice.

The law neither can nor does attempt to discriminate between different schools of practice, nor determine which school has the better methods. The law does, however, recognize the fact that in

all schools the practice of medicine and surgery is now highly specialized. The general practitioner is not required to be in any branch of practice all that a specialist in that branch can be. Nor is a practitioner in a country district expected to possess the knowledge or skill of one who lives in a centre of population with larger opportunities to see and to learn.

On the other hand, a specialist is held to a higher standard, and is bound to exercise that knowledge and skill that practitioners in his special line may reasonably be expected to have.

While the patient cannot be expected to have that discriminating knowledge which will enable him to determine to which class of specialists he should submit himself for treatment in every particular case, he yet is held to know certain broad distinctions. He is not entitled to insist upon homœopathic treatment from a regular physician, or *vice versa*. If he puts himself under the care of a Christian Science healer, he cannot reasonably complain if the treatment does not continue to be effective. If he consults for his own ailments one of that class of specialists who devote themselves to the treatment of the diseases of four-footed patients, he will have only himself to thank and to hold responsible if his doctor should fail to display horse-sense in his treatment. This principle is illustrated by one of the oldest-reported cases of malpractice, a Mahomedan case, where "a man, who had a disorder in his eyes, called on a farrier for a remedy; and he applied to the eyes a medicine commonly used for *his* patients; the man lost his sight, and brought an action for damages; but the judge said: 'No action lies, for if the complainant had not himself been an ass he never would have employed a farrier.'"

On the other hand, the practitioner should recognize the fact that the specialization of his profession is the necessary result of the increase of knowledge beyond the limitations of human capacity, and that it is not possible for any mortal man to know all that can at any given time be known in every branch of medicine and surgery. The doctor should, therefore, unless in a case of emergency, where the aid of a specialist is not immediately available, refuse to assume the grave responsibility of undertaking to treat that which can, with reasonable certainty of benefit to the patient, be better treated by a specialist. Under such conditions, the doctor's rashness will render him liable in damages if injury to his patient result from the treatment.

The law does not presume that every practitioner possesses the greatest possible knowledge, nor the highest possible skill. The law recognizes the fact that the accidents of fortune deny to equal merit equal opportunities to gain experience and to acquire that skill which only experience can add to knowledge; and that, given equal educational advantages, equal experience, and equal desire to become skilful, the difference in the personal equation will always

distinguish one man from another. The test is, therefore, the doctor's possession of that degree of knowledge, intelligence, carefulness, and skill which may be reasonably expected of an average practitioner of the particular school under the conditions of his environment.

The maximum of professional efficiency changes from day to day with the progress of discoveries in science, and with improvements in methods of treatment and of operation. The use of anæsthetics, general and local; antiseptic precautions in operating; the germ theory of disease; the development of sanitary science; the administration of antitoxins; the disappearance of the bleeders and cuppers; the diminutions in doses of medicines; the general employment of trained nurses; and the specialization of the profession, are a few illustrations of the changes which have come in the lifetime of men now living, and which have forced themselves upon the attention of even unobservant laymen. That system and those appliances whose use would, but a few years ago, have been regarded as a fulfilment of the doctor's duty to his patient, would to-day be universally held to fall far short of an adequate performance of that duty. No man can doubt that the future has further advances in store. But a doctor cannot be required to use immediately upon its appearance every new remedy or appliance that may be brought to his attention. The suggested improvement must have passed beyond the stage of experiment, and, even if its applicability be clear in theory, that probable sufficiency must have received the seal of an established practical efficiency before the doctor can be held to be negligent because of a failure to employ it. The test is, whether or not the particular method of treatment or operation is of recognized efficacy, and in general use by careful practitioners of the particular school under like conditions.

That rule which the law expresses in the maxim "*Respondeat Superior*" applies to medical men. Every doctor is, therefore, held to liability for the acts and omissions of his agents. The term "agents" includes assistants employed by the doctor and brought into the case by him to assist him in the treatment or operation; but it does not include consultants or specialists, practising independently, though nominated by the doctor and brought in at his instance; nor does it include those ministering angels of mercy, the trained nurses, now employed so universally and with such beneficial results; nor does it include the apothecary by whom the medicines prescribed by the doctor are supplied. The consultant, the specialist, the nurse, and the druggist are all "independent contractors," and each is held liable for his own negligence, and the doctor is not held liable for the negligence of any of them, unless it be shown that, if selected by him, he has been negligent in their selection; or, in other words, that the individual selected is so generally known to be incompetent that a person of reasonable care-

fulness would not have selected him or her. If, however, any of those "independent contractors," whether or not selected by the doctor in charge, should, subsequently to their selection, so manifest their incompetency that a doctor of reasonable skill ought to be aware of it, the doctor will be held to be negligent if he does not insist upon the removal of the incompetent.

In addition to bringing to the service of his patient his knowledge and skill, the doctor must also be as frequent and as long-continued in his attendance as the necessities of the case require; and when he ceases his visits he must give such directions as may be necessary for his patient's conduct and manner of life under the conditions of convalescence.

Any shortcoming on the doctor's part or on the part of any agent of his, in the exercise of reasonable knowledge, intelligence, and skill, in faithful attendance, in the selection or retention of independent contractors, or in necessary advice as to precautions to be taken by the patient in the future, will constitute negligence, and will subject the doctor to a possibility, not only of a forfeiture of his professional compensation, but also of a liability in damages for malpractice.

The gravamen of the action being negligence, a doctor cannot be held liable for an honest mistake in the exercise of judgment or for a failure to rise to the height of an emergency, if he has done all that a physician or surgeon of average knowledge and skill could reasonably be expected to do under the circumstances. This principle may find an illustration when, in the course of an operation for one cause, there is discovered another cause, for which further or other immediate operation may be imperatively necessary. Under those conditions the surgeon is called upon to assume a grave responsibility. The patient's consent to the primary operation does not necessarily include an implied consent to a secondary operation. Nevertheless, the surgeon must courageously do that which he believes to be best for his patient, whatever it be, and trust that the law will protect him.

In every case and at every stage of the case where a choice has to be made between courses of action, whether the subject for decision be a reference to a specialist, or the calling in of a consultant, or the continuance of undivided responsibility, or a change in the treatment, or an exploration, or an operation, either original or secondary, the doctor should ask himself what, with his knowledge of the conditions, he would, if he were the patient, insist upon. That self-inquiry will not relieve the doctor from liability, if, in his answer to it, and his consequent action, he sins against knowledge; but it will, if the question be fearlessly answered, save the doctor, in most cases, from mistakes that will be hurtful to the patient, and may be injurious to the doctor's reputation.

An action for malpractice, whether well or ill founded, is a great

injury to a professional man; and the law puts upon the patient who makes such a charge the burden of proving by a preponderance of evidence that the doctor has failed in the performance of his duty; for the presumption in the case of one who has been legally licensed to practice is that he was duly qualified, and that that which he has done was rightly done. Of course, the doctor cannot be held responsible if the patient fails to obey the doctor's directions or undertakes to act upon his, the patient's, own judgment as to the treatment.

In cases of malpractice, the damages, if any be awarded, will generally be compensatory in character, and will be measured by the injury to the plaintiff directly caused by the doctor's negligence, and resulting in bodily pain and suffering, present or prospective, in injury to health, in diminished physical or mental capacity, in loss of present or future earnings, and in actual expenditures, or legal liability incurred, for subsequent medical or surgical treatment, but not including counsel fees, nor interest upon the damages accruing prior to the verdict therefor. When the injured plaintiff is a wife or child, an action may be brought on her or his behalf, and the husband or parent may also sue on his own behalf, and recover, when the injured patient is a wife, damages for the loss of his wife's society and services; and where the injured person is a child or servant, compensation for the loss of services during the time of service or during the minority of the child.

Where the doctor's malpractice causes the death of the patient, those in whom a statute vests a right of action may recover damages based upon the material, but not the sentimental, loss to the plaintiffs caused by the death. Exemplary damages, which are damages in amount more than compensatory, will be given only where the evidence clearly shows that the doctor has acted wantonly or perversely, and with such criminal indifference to his obligations as to amount to proof of a wrongful intent.

When a doctor's treatment or his exercise of care is questioned in a legal proceeding, the propriety of that treatment and that care can only be determined by a consideration of the testimony of other practitioners as to the conformity of that treatment to established methods, and as to the sufficiency of the doctor's exercise of care under the particular conditions.

It is probable that actions for malpractice will be more frequent in the future than in the past. The increase in recent years in the number of lawyers dependent for their living upon the profits of their practice, and the consequent stress of competition, have enlarged that class of legal practitioners who, like Dodson and Fogg, of immortal memory, take cases on "spec," and charge nothing unless they make it out of the defendant, and who, too often, promote litigation, and win their cases by the careful coaching of their witnesses. Such pirates make the large employers of labor their chief victims; but they naturally are keen to discover any persons whom

they can either frighten into the payment of blackmail or from whom they can recover verdicts which, when paid, go largely into the pockets of the successful pettifogger. Therefore, the physician, and still more the surgeon, should, for his own protection, take such prudent precautions in obtaining the patient's consent, and having available such proof of the correctness of the treatment, as will guard him most effectually against a possible claim.

The doctor will be brought into contact with the criminal law if he violates any statute which authorizes an indictment and which imposes a penalty. A doctor may also be held responsible to the criminal law for the death of a patient, if that death has been directly caused by the doctor's want of ordinary professional knowledge or want of ordinary attention in his care of his patient; and, in such a case, the doctor's intention to cure his patient will not relieve him from the consequences of his foolhardy presumption. Criminal statutes are strictly construed, and their legal effect depends upon their precise terms. In a criminal case, the presumption is that the defendant is innocent until he has been proved to be guilty by evidence excluding any reasonable doubt.

No class of men render as much or as valuable gratuitous service as the members of the medical profession; yet the law sometimes is called upon to deal with the question of the doctor's compensation. The old theory was that the doctor's fee is an *honorarium*, and, if unpaid, is not a subject of collection by law. The modern theory is that the services of a doctor when charged must be paid. If the amount of that compensation has been fixed by pre-contract, that contract will be enforced. If no contract has been made, a recovery in law may be had upon the basis of that which is reasonable, taking into consideration the professional rank of the doctor, the character of the services rendered, and the amount of compensation usual in the locality for such services so rendered, but not taking into consideration the greater or less pecuniary responsibility of the patient. The proof of the reasonableness of the doctor's compensation may be made by the testimony of other doctors. The patient may resist payment, either by disputing the fact that the services sued for were rendered, or that they were of the character claimed, or by proving that there was malpractice on the part of the doctor.

It is to be noted that in many jurisdictions, in the administration of the estate of a decedent, the expenses of his last illness, including both medical attendance and nursing, are held to be preferred claims.

The doctor is also brought into touch with the law as an expert witness. He may be called to testify as to the results of an autopsy, or as to the nature and effect of an injury or a wound, or as to the sanity or insanity of a person, who is accused of crime, or is a subject of present or prospective confinement in an asylum, or as to the testamentary capacity of one who has made a will, or as to the

sufficiency of another doctor's method of treating a patient, or as to the proper amount of another doctor's professional compensation.

As long ago as 1553 Mr. Justice Saunders said: "If matters arise in our law which concern other sciences or faculties, we commonly apply for the aid of that science or faculty which it concerns;" and he added, with that diffident complacency and that shrinking modesty which from that day to this has ever distinguished judges and lawyers, "this is an honorable and commendable thing in our law, for thereby it appears that we do not despise all other sciences but our own, but we approve of them and encourage them as things worthy of commendation."

The general rule is that when in any legal proceeding there comes into question any subject which is "beyond the range of ordinary observation and intelligence," a person who is skilled in that particular subject may be summoned as a witness to inform the court and the jury as to it; and, of course, when the question is medical or surgical in character, a doctor may be called to testify.

The term "witness," in its primary meaning, is "one who sees or knows, personally," and, in its secondary meaning, "one who gives testimony or evidence."

It is clear that an expert is not a witness within that primary meaning. He has no knowledge as to the facts in controversy. On the other hand, he does know that which the judge and the jury cannot know, and that is the scientific inferences that may properly be drawn from the facts proved. In other words, the duty of the expert is to do, with regard to inferences which are "beyond the range of ordinary observation and intelligence," precisely that which the average man can do for himself as to inferences which are within that range. Properly speaking, therefore, the function of an expert is not that of a witness, but it is that of an assessor, that is, of one who sits by the judge and gives him the benefit of his advice.

It would be more in keeping with legal theory if the law, instead of permitting each party to a cause to call his expert as a witness, would authorize some competent appointing power to select an expert, to be adequately paid by the State, to sit with the judge, and, as an assessor, to impartially instruct the jury as to the technical questions in the case, in the same way that the judge instructs the jury as to the law. If that were the practice, we should avoid that suspicion of prejudicing partisanship, which is always suggested by the sight of an expert witness, known to have been called and to be compensated by one side, and to be engaged, not only to state his views on behalf of the side which has called him, but also to assist the counsel for that side in the cross-examination of the expert witnesses who are called by the other side. This plan would, however, involve certain practical difficulties. In the first place, if the appointment were made by political officers, considerations other than those of professional competency would probably deter-

mine the selection; and if the appointment were made for each case by the judges, the professional qualifications of the appointee might or might not be so generally recognized as to render the selection satisfactory to all parties to the proceeding. In the next place, there would be no possibility of appeal from the conclusions of the expert, or of correction of any erroneous views which he might express; for neither the judge at the trial, nor an appellate tribunal, would be competent to review his instructions. It is, therefore, probably safer to adhere to the present system, under which the conclusions of the expert can be tested by cross-examination, and have only such weight with the jury as their force and clearness of statement and their soundness of reasoning may secure for them.

It has sometimes been questioned whether or not a medical expert can be compelled to obey a subpoena, and for the ordinary and merely nominal fees of a witness give to the court and the party calling him the benefit of his testimony as an expert, when that testimony derives its value from an expensive education and from years of study and experience, and when his attendance in court may, possibly, lose him profitable business. The better opinion would seem to be that as the duty of a citizen requires him to obey, without cavil or question, the process of a court, any doctor, if duly summoned by service of a writ of subpoena, and by payment or tender of the regular witness fees, if he demands them, may be compelled to attend the court and to answer any questions that may be asked him; but he cannot be compelled in that manner to give any consideration to the subject matter of examination elsewhere than on the witness stand. Therefore, as it is one thing to take a horse to water and another and a different thing to make him drink, so it is one thing to bring an unwilling expert into court and another and a different thing to draw from him that clear and convincing testimony which will aid the cause of the party in whose behalf he has been summoned. No competent lawyer, therefore, would call an expert to testify without making satisfactory arrangements as to that expert's compensation.

As a doctor can be compelled by a subpoena to appear and testify, it follows that in the absence of an express contract of compensation he cannot legally recover as compensation more than the ordinary witness fees, and, therefore, it is wise for the doctor, when he is asked to serve as an expert, to have a clear understanding as to the amount of his compensation, and as to the responsibility of the party by whom payment is agreed to be made.

There are experts and experts. It is desirable, in the first place, that the doctor should not only know his subject accurately and thoroughly, but also that he should have sufficient decision of character and power of repression and of expression to enable him to meet the test of a searching cross-examination, and to make his view clear and convincing to the minds of men of not more than,



and often less than, average intelligence. He should be sparing in the use of technical terms, and when he does use them he should translate them, so that their meaning may be grasped by the court and jury. Above all, while firm and self-respecting in his manner, he should avoid all appearances of dogmatism and intolerance. If long and involved hypothetical questions are put to him, he should not answer hastily, but should insist, as is his right, upon full time to consider the question before answering, and to satisfy himself that no false analogy, nor any snare for the unwary, lurk within its many words. The doctor whose knowledge is real and who thinks clearly and talks plainly has nothing to fear from any cross-examination, however severe; and he will be treated by both the court and the counsel with the most distinguished consideration.

The doctor may also bring himself into contact with the law by certifying erroneously as to the insanity of a patient, who, upon that certificate, is committed to confinement. While a mistake in judgment or an error in diagnosis will not subject the doctor to any liability, yet a misstatement of a material fact will render the doctor liable in damages. Doctors should scrutinize with care every word of printed forms submitted in such cases for their signature; and they should carefully examine, or have a lawyer examine for them, the statute under which they are asked to certify.

From all this there follow three practical conclusions:

In the first place, it is the duty of every good citizen to obey the law, and this duty is in a high degree incumbent upon members of all learned professions whose education and training may properly be supposed to raise them above the common mass of people, and to give to them a higher sense of duty. If, therefore, there be in the law any regulation which seems to you to do injustice to the interest of your profession, or to yourself, work and agitate for the reformation of the law; but, so long as the regulation be in force, faithfully obey it.

In the second place, remember that it is as foolish for a medical man to undertake to determine for himself what the law is upon any subject as it is for a lawyer to attempt to prescribe for the bodily ills of himself or of any other person. Therefore, whenever you are in any way brought face to face with law, consult a lawyer, and do it promptly, for it is as true in law as it is in medicine, that "an ounce of prevention is," if it be not too late to prevent, "better than a pound of cure."

In the third place, as legal restrictions and professional ethics touch at many points, it is wise for every young doctor to form such relations of mutual confidence and regard with one or more of the seniors of his profession, that he can obtain for himself the great benefits of a senior's advice, when questions of professional expediency present themselves. Remember that every profession has its

traditions, in which is crystallized the wisdom of its past; and that seniors who have risen to eminence and who have that soundness of judgment which the young, however learned and able, rarely have, can best determine when it is and when it is not judicious to depart from those traditions.

And one word more: I envy you; not only because you are young and I am old, for the old always envy the young; but also, and chiefly because you are to enter upon the practice of the greatest of the professions; a profession whose members have it in their power to do more than other men in relieving human suffering and alleviating human misery; a profession whose history is a story of continued growth and progress, of brilliant discoveries in science and beneficent improvements in methods of treatment and of operation, and, in many instances, of martyrdom to duty.

I close with the expression of the hope that you will walk worthy of your high vocation, and that in the years to come you will be loyal to your Alma Mater and do honor to your profession and your College.

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## SOME OBSERVATIONS ON ANEURYSM AND ARTERIO-SCLEROSIS.<sup>1</sup>

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### HISTORY.

In tracing the history of the study of aneurysm, we find it divides itself into two periods. First, that in which the aneurysm was looked upon as a localized disease of the vessel; second, that in which arteriosclerosis was recognized, aneurysm being considered in association with an advanced stage of this change in the arterial wall.

The first of these periods, that of aneurysm, divides itself into two—that in which the peripheral aneurysm was recognized and treated, and that in which the deep seated, like the thoracic aneurysm, was recognized.

The steps in the development of our present knowledge of arterial disease as they are here presented will be appreciated by following these charts.

<sup>1</sup> The Mütter Lecture, delivered before the College of Physicians of Philadelphia.

## CHART I.

## Historical Chart. (Chronological.)

## A. Epoch of Ancient Medicine (1500 B.C.-210 A.D.).

Egyptian Medicine.

Assyro-Babylonian Medicine (Ignorance and Superstition).

Hebrew Medicine (1500-400 B.C.).

Indian Medicine.

Greek Medicine (400-300 B.C.)

Hippocrates (460-377 B.C.) } Aneurysm confused with other tumors.

Aristotle (384-323 B.C.) }

School of Alexandria (300 B.C.).

Roman Medicine (100 B.C.-210 A.D.).

Asclepiades (100 B.C.).

Celsus (First Century).

Galen (131-210 A.D.). (Term "Aneurysm"—"widening." Arteries contain blood, not air.)

The epoch of ancient medicine, which may be said to extend from 1500 B.C. to 200 A.D., is represented by Egyptian, Assyro-Babylonian, Hebrew, Indian, Greek, and Roman medicine. In this epoch, doubtless, peripheral aneurysms were seen but confused with tumors of other nature. In Greek and Roman medicine occur the names of Hippocrates (460-377 B.C.), Aristotle (384-323 B.C.), Herophilus and Erasistratus of the school of Alexandria (300 B.C.), Asclepiades (100 B.C.), Celsus (first century), Aretaeus (second century), and Galen (131-210 A.D.). It is the last-named who probably makes the first definite reference in literature to the condition and who used the term *Ἀνέυρυσμα*, meaning a dilatation.

It will be remembered that it was Galen who declared that the arteries contained blood not air, the latter view having been held by Erasistratus of the school of Alexandria. (Dezeimeri's *Dictionnaire Historique de la Médecine Ancienne et Moderne*.) The translation of the passage from Galen's work in which he refers to aneurysm is the following: "When the mouth of the artery is opened the affection is called *Ἀνέυρυσμα* (dilatation). The same thing happens when the artery being wounded, the incumbent skin is cicatrized, but the wound of the artery remains, being neither conglutinated, covered with a cicatrix, nor shut by incarnations. Affections of this kind are known by the pulsation of the arteries, or more especially by compressing the artery, for then all the tumor disappears, the matter that caused it recurring into the artery." This was written in the latter part of the second century. (Quoted by Robert James in *A Medical Dictionary*, 1743, under "Aneurysm.")

## CHART II.

## Mediæval Medicine (300-1400 A.D.).

Byzantine Medicine.

Oribasius (326-403 A.D.). Recognized peripheral aneurysms.

Paul of Ægina (625-690 A.D.). Recommended ligation of brachial artery for aneurysm at bend of elbow.

Arabian Medicine.

Avicenna (980-1036 A.D.). Writes on peripheral aneurysm.

The next epoch, that of mediæval medicine, which may be said to extend from 200 to 1400 A.D., and which consists of the Byzantine (300-700) and Arabian (800-1000) periods, also the school of Salerno (1000-1200) and that of Mundino (Mundinus) (1276-1326), contains but indefinite reference to peripheral aneurysms, though in the Byzantine period, Oribasius (326-403) ligated arteries for cure of aneurysm, and Paul of Ægina (625-690) recommended ligation of the brachial artery a few fingers' breadth below the axilla for cure of aneurysm at the bend of the elbow (Hodgson), and in *Arabian Medicine* we find that Avicenna (980-1036) was familiar with peripheral aneurysms. Most authors attribute the first recognition of peripheral aneurysm to Avicenna, though from the above it is evident that these aneurysms were recognized and even treated four or five hundred years before Avicenna.

In these periods, however, all of those fundamental facts of gross anatomy and physiology were being sought for, so that beyond a few observations of historic interest these periods contain no contributions to our knowledge of arterial disease. Until anatomy was systematically studied, this whole subject remained in obscurity. The advances in anatomy, indeed, amounted to very little up to this time, the beginning of the epoch of modern medicine which begins with the time of Linacre (1461-1524) and extends to our own. Prior to this (1400) the studies of human anatomy may be estimated by the fact that Mundino (1276-1326), who was professor of anatomy at the University of Bologna during the latter part of the thirteenth century, "dissected in eleven years only three human bodies." From the period of the Alexandrian school (300 B.C.) to this time of Mundino (1300 A.D.) the human body had never been dissected (Chapman). With the beginning of the sixteenth century, peripheral aneurysms were well recognized, Paré (1517-1590) introducing the method of ligating on both sides of the aneurysm, allowing, however, the intervening area to slough out. He also definitely differentiated abscesses from aneurysms.

The discussion now turns to the possibility of aneurysms of deep-seated vessels. To Vesalius (1514-1565) is due the credit of making the first diagnosis of intrathoracic aneurysm during life. This aneurysm followed injury and was detected by examining the back of the patient; a point of great clinical importance rarely mentioned, and one alluded to in a recent paper by Osler.

"The Doctrine of Dilatation of the Aorta," however, made so slow a progress that in the year 1596 when Sylvaticus published his "Treatise on Aneurysm" he did not mention internal aneurysm, and many years afterward (1658) Riolanus asserted that "aneurysm happened but seldom in the trunk of aorta in consequence of the thickness of its parietes." Elsnerus prefixed to his observations concerning aneurysm of the arch of the aorta *De Paradoxico Aneurismate*. The *Sepulchretum Anatomicum* of Theophilus and the

*Historia Anatomica Medica* of Lieutaud, Morgagni characterized as "unsystematic and vague."

Of thoracic and deep-seated aneurysm Morgagni says: "From the year 1670 they ceased to be considered as rare occurrences; and we have now acquired such familiarity of the disease from its causes and symptoms that we believe it may be distinguished, even when very small, and entirely concealed within the thorax." Malpighi, who was partly a contemporary of Morgagni "accounted the knowledge of dilatation of the aorta among the improvements of (his) age."<sup>1</sup> About this time (1670) Valsalva (1666-1723) tied the carotid of dogs repeatedly, and in one instance he tied both carotids, the dog living twenty-two days (Hodgson).

Much valuable clinical and pathological information was added by Johannes Mariana Lancisi (1654-1720) in his *De Motu Cordis et Aneurismatibus*, and by Haller (1708-1777), who in his *Opuscula Pathologica* (vol. x. and book vii., p. 127) introduces the term "Atheroma" and demonstrates collateral circulation, also by John Hunter (1728-1793), who tied the distal end of the vessel for cure of aneurysm (1785).

In the writings of Malpighi (1628-1694), Valsalva (1666-1723), and Morgagni (1682-1771), as embodied in his *De Sedibus et Causis Morborum*, published in 1760, are systematic ante-mortem and post-mortem descriptions of aneurysm. Here we find accurate reports of aneurysm of the splenic, popliteal, and inguinal arteries. Of arteries in general we find reports on ulceration of the coats of the vessel. Of the aorta we find reports on atheromatous coats, thickening and induration, inflammation, opaque spots, ossification, callous, cartilaginous deposits, incipient aneurysm, advanced aneurysm, and ruptured aneurysm. Case 26 is the report of sudden death resulting from rupture of one of the coronary arteries.

In 1805 Sir Astley Cooper ligated the carotid artery, a step which, as already stated, had been taken by Valsalva experimenting upon dogs. In 1811 Joseph Hodgson contributed his *Treatise on the Disease of the Arteries* which contains observations upon the pathology and treatment. Antonio Scarpa (1748-1832) also published an exhaustive *Treatise on Pathology and Surgical Treatment of Aneurysm* which was translated into English from the Italian about 1830. The clinical contributions of Laennec (1781-1826) and of that great teacher Louis (1787-1872) must not be omitted. From Corvisart (1755-1821) we get the term "vegetation."

Peripheral aneurysms then were recognized and treated as far back as the third and fourth centuries. Deep-seated aneurysms were recognized about the end of the seventeenth century.

<sup>1</sup> Seats and Causes of Disease, xviii., 14; Cook's translation, 1824, p. 330.

## CHART III.

## Historical Chart. (Chronological.)

## Modern Medicine (1400-1900 A.D.).

Revival of Anatomy. Vesalius (1514-1565). Thoracic aneurysm diagnosed during life.  
 Practical Surgery. Paré (1517-1590). Ligates on both sides of aneurysm.

Circulation. Vascular system including capillaries demonstrated.

Harvey (1578-1657). Circulation.

Malpighi (1628-1694).

Van Leeuwenhoek (1632-1723). } Capillaries.

Gross. Pathology.

Morgagni (1682-1771)

Malpighi (1628-1694)

Valsalva (1666-1723)

} Peripheral and deep-seated aneurysm and other diseases  
 of the arterial wall recognized and described.

## Medical, Surgical, and Pathological.

Lancisi (1654-1720). "De Motu Cordis et Aneurysmatibus."

Haller (1708-1777). Term "Atheroma."

Auenbrugger (1722-1809). Percussion.

John Hunter (1728-1793). Ties distal end for cure of aneurysm.

Astley Cooper. Ligates carotid (1805).

Scarpa (1748-1832). "Treatise on Pathology and Surgical Treatment of Aneurysm."

Joseph Hodgson. "Treatise on Pathology and Treatment of Aneurysm" (1811).

Corvisart (1755-1821). Term "Vegetation."

Laennec (1781-1826). Auscultation.

Abernethy. "Origin and Treatment of Aneurysm" (1817).

Coming more to our own times, we find the observations upon the diseased arteries more specific as indicated by such terms as "arteriosclerosis" introduced by Lobstein in 1834 and "endarteritis obliterans" by Friedländer. "Arterio-capillary fibrosis" was introduced by Gull and Sutton, who recognized the condition as an independent affection.

The first theory upon which arterial disease was studied was that of inflammation, a view held by such men as Scarpa, Haller, Kreysig, Lobstein, and Bizot. It must be remembered, however, that at the time of these observers no very clear view of the pathology of inflammation existed, and consequently one obscure subject was being explained by another, almost equally obscure.

In 1844 Rokitansky opposed the inflammation theory and offered in its place the hypothesis, that material detrimental to the tissues of the arterial wall was deposited from the blood stream. Opposed to this view were Engel, Crisp, and Neumann, while Donders and Jansen were in support of the Vienna pathologist.

The important studies from this point on, as the microscope and histological technique improved, were concerned with the minute anatomy of the bloodvessels, also the physical laws governing their degree of dilatation, elasticity and resiliency.

Resse, a strong opponent of Rokitansky, presented important histological observations in support of the theory of *interrupted nutrition* and new connective-tissue formation.

It was Virchow, however, who was the strongest opponent, and to him is attributable the complete overthrow of the humero-

pathological doctrine of Rokitansky. Virchow divided the process into two: first, a simple degeneration; second, an atheromatous degeneration. The first he considered as a passive occurrence, while the latter he looked upon as an active formative process. The hyperplasia of the intima he regarded as any other chronic inflammatory process. The sclerosis he considered to be a chronic inflammation, as had Dittrich before him, and to it he gave the name "endarteritis chronica deformans."

With the advance in the knowledge of the minute anatomy of the vessel wall, but more especially of the pathology of inflammation made in consequence of Cohnheim's and Metchnikoff's observations, new questions arose, such as, "What is the relation of the vasa vasora to the inflammatory area, and what part do the white corpuscles play in the process?" and "How do they reach the non-vascular intima directly, from the blood circulating in the lumen of the vessel or from the vasa vasora?" At or about this time much emphasis was laid upon high blood pressure as a result of continued contraction of the arterioles.

Traube was the chief supporter of this the "mechanical theory," while Rindfleisch suggested that disturbances of nutrition from slowing of the current were responsible for the disease of the wall. These were, however, only hypotheses. By careful histological search, in which they failed to find any means of communication between the non-vascular intima and vascular other coats, Götze, Koester, Stronganow, and Talma concluded that the intima became affected from the blood circulating in the lumen of the vessel. Koester, together with Friedländer, and before them Virchow, proved that cells do pass from the vasa vasora to the intima. Trompeter and Krafft, scholars of Koester, now made the following important contributions:

1. The media is always involved at or about the same time as the intima (mesarteritis).

2. That the vasa vasora play an essential part in the process of disease of the vessel wall.

3. They contributed also important anatomical facts.

Shortly after this the importance of the vasa vasora in their relation to the nutrition and disease of the vessel wall was shown by Durante's experiment.

These experiments showed that stopping the circulation of the blood in the lumen of the vessel was followed by no damage to the vessel wall, while cessation of blood flow in the vasa vasora was followed by destruction of the vessel wall.

Thus, while many isolated facts of great value had been contributed, yet no very clear knowledge of the etiology and sequence of events in this prevalent disease up to this time existed.

Thoma, as a result of his studies, presented an entirely new theory based largely upon histological and clinical observation.

Thoma's studies were on three conditions:

1. Vessels in the foetus and newborn.
2. Vessels in the stump of an amputated limb.
3. Vessels showing disease.

In the first of these, the foetus and newborn, he observed that the obliteration of the umbilical blood track (Nabelblutbalm) proceeds by way of a thickening of the intima.

In the second (the vessels in the amputated stump) he observed also that obliteration of the vessel took place by a thickening of the intima. He concluded that this thickening took place in order to compensate for the lessened amount of blood consequent upon the cessation of circulation through these vessels. These he called "Physiological Thickenings."

In the third, arteriosclerosis, he finds the same factors as in the physiological process, but appearing in different sequence. He distinguished two processes in the diffuse form of arteriosclerosis.

1. Primary.
2. Secondary.

In the primary he finds a yielding of the vessel from loss in elasticity with a consequent widening of the vessel and slowing of the blood current. Connective tissue develops in the subendothelial layers of the intima, a process which tends to restore the relation between the vessel and its contents. Slowing of the current may in itself disturb the relation between vessel and contents and so require a compensatory thickening of the intima.

With advancing years in an individual the slowing of the blood current is, *pari passu*, met by this compensatory thickening, and the relation between blood stream, vessel wall, cardiac potentiality and blood pressure is thus maintained. It is certainly a beautiful theory.

In the secondary variety the process begins in the small vessels. In arteriosclerosis nodosa the diseased areas are considered as localized points of elastic weakening, the compensatory process taking place at these points. The twisting of the vessel Thoma considered as points of diminished elasticity yielding to blood pressure. We, therefore, have the circumscribed or nodular form (of Councilman) and the diffuse form, for both of which we have the explanation that there is a primary weakening of the elastic coat with dilatation and compensatory thickening of the intima by development of connective tissue between the endothelium and underlying elastic tissue.

Many are the supporters of Thoma's theory, among these being von Schrötter, who, in *Nothnagel's System*, declares the explanation as final.

On the other hand, there are those who oppose the view, as Beneke and Pekelharing, for example, who differ from Thoma in considering a disproportion between pressure and tension and diminished resistance to be primary factors.



Marchand, too, considers that the many cases of circumscribed involvement of the intima with an almost normal media argue against a uniform compensatory intima thickening, and Bollinger asks, "Is not the mechanical theory too much considered?"<sup>1</sup>

R. F. Fuchs is perhaps the most active opponent of Thoma's theory. He considers that it is difficult to prove that an initial slowing of the blood current occurs and declares that it is unreliable to build a theory upon an unknown and undeterminable foundation.

The French writers, of whom Huchard is the most prominent, consider the process as one not confined to the vessels but a systematic condition manifesting itself in the vessel wall as in the kidney, the liver, and elsewhere.

#### CHART IV.

Theories. Nineteenth Century. (Not Chronological.)

- |  |   |
|--|---|
| I. Inflammation theory.  | Many observers.   |
| Pathology of Inflammation not clearly understood.  |   |
| II. Humero-pathological theory, 1844.  | Rokitansky.   |
| III. Pathology of inflammation.  | Cohnheim.   |
| Better understood.   | Metchnikoff.  |
| IV. Mechanical theory  | Traub.  |
| V. Interrupted nutrition theory.   | Rindfleisch.  |
| Question 1. Nutrition of vessel wall?  |   |
| "    2. Passage of leukocytes into vessel wall from lumen of vessel or from vasa vasora? |   |
| "    3. Nutrition of non-vascular intima?  |   |
| VI. Passage of leukocytes from lumen hypothesis.   | <div style="display: inline-block; vertical-align: middle;"> <div style="display: inline-block; vertical-align: middle;"> Gütte,<br/>Koester,<br/>Stronganow,<br/>Talma. </div> <div style="display: inline-block; vertical-align: middle; font-size: 3em; margin: 0 5px;">}</div> </div> |
| VII. Nutrition from vasa vasora <i>only</i> , demonstrated.                              | Durante.  |
| VIII. Passage of leukocytes from vasa vasora to non-vascular intima, demonstrated.       | <div style="display: inline-block; vertical-align: middle;"> Virchow,<br/>Koester. </div> <div style="display: inline-block; vertical-align: middle; font-size: 3em; margin: 0 5px;">}</div>  |
| IX. Compensatory process and molecular theory.   | Thoma.  |

For further details see Prof. Jones' monograph on "Arteriosclerosis," to which I am indebted for much valuable information.

#### CHART V.

Nomenclature. Nineteenth Century. (Not Chronological.)

Arteriosclerosis . . . . .	Lobstein.
Arteritis.	
Atheroma . . . . .	Haller.
Arterio-capillary Fibrosis . . . . .	Gull and Sutton.
Periarteritis.	
Periarteritis Nodosa, 1866 . . . . .	Kussmaul.
Obliterative Endarteritis, 1876 . . . . .	Friedländer.
Endarteritis, Chronica Deformans . . . . .	Virchow.
Endarteritis Nodosa or Conscripta Diffusa . . . . .	Councilman.
Mesarteritis . . . . .	Trompeter-Krafft.
Angiosclerosis . . . . .	Thoma.

Subdivisions of aneurysms not given, as these refer more especially to gross than to histological appearances.

## CHART VI.

## Epochs.

Prior to 400 B. C.	. . .	Complete ignorance.	
400 B. C. to 300 A. D.	. . .	Beginning of accurate observation.	ANATOMICAL FACTS.
300 to 1500	. . .	Decline of Anatomic study.	
		Superstition and prejudice.	
1500 to 1600	. . .	Revival of ANATOMY.	
		Anatomical Laboratories.	
1600 to 1700	. . .	PATHOLOGY.	
		Pathology (Gross).	
		Pathological Laboratories.	
		SYMPTOMATOLOGY and Morbid Pathology.	
1700 to 1800	. . .	Methods of PHYSICAL EXAMINATION.	CLINICAL.
1800 to 1900	. . .	PATHOLOGICAL HISTOLOGY.	
		BACTERIOLOGY.	
		PHYSIOLOGICAL CHEMISTRY.	

Each of the above represents the dominant consideration of its time.

Such, then, is the history of the work done upon the arteries from the earliest epochs of medicine to our own times. It represents a vast expenditure of thought by the very ablest scientific thinkers, especially of the last three centuries.

There yet remain unanswered many questions, from among which the following have been selected, with the hope that some facts may be presented which may prove suggestive to other observers, stimulating them to investigate this widespread and important disease.

The questions are:

1. Arterial disease in animals.
2. The earliest age in which arterial disease occurs in man, and at what age it is most common.
3. The teratological factor.
4. The relation of syphilis and pulmonary tuberculosis to aneurysm.
5. Relative frequency of aneurysm in the white to colored races.
6. Relation of arteriosclerosis to aneurysm.
7. The physical properties of the arterial wall.
8. The nature of the change in the elastic tissue, which is conceded to be the most important in arterial disease.

## ARTERIAL DISEASE IN ANIMALS.

The determination of the presence or absence of arterial disease in animals presents many points of interest, such as the influence of strain, as in the beasts of burden; the influence of disease peculiar to man, as syphilis; the relative elasticity of the animal's vessel and that of man, etc.

The animal's vessel possesses a greater degree of elasticity, and this may enable the vessel to withstand strain for a longer time without yielding. This offers a fruitful field for work. Horses, and more especially asses, are subject to aneurysm of the superior mesenteric and aorta due to a parasite—the *Strongylus Armatus*.

Many authors state that peripheral aneurysm is practically unknown in domestic animals.

Pigs and dogs are stated to be occasionally the subjects of aortic aneurysm.

I examined the aortas of 103 domestic animals without finding any evidence, *in the gross*, of arterial disease.

In the aorta of the steer there occurs just beyond the first portion of the arch a thickening which is, however, not pathological. This is occasionally found in man.

EARLIEST AGE AT WHICH ARTERIAL DISEASE OCCURS IN MAN  
AND THAT AT WHICH IT IS COMMONEST.

It is generally stated that arterial disease in children is rare, but no definite age limit is given. Thus, Keating says: "Endarteritis with degenerative changes seems to be a rare affection in children; it would appear that the bloodvessels of the brain, and the walls of the aorta are the points chiefly affected, although other large vessels are occasionally the seat of atheroma." (*Cyclopedia of the Diseases of Children*, Keating, vol. ii. p. 874.)

Schmidt, however, reports a radial aneurysm in an infant eight weeks old; Syme, a popliteal aneurysm in a boy, aged seven years, and Hodgson an aneurysm of the carotid in a girl, aged ten years.

R. W. Parker says: "After careful search of the literature," he found only 15 cases of aneurysm in those under twenty years.

Through the courtesy of Dr. Mathias Nicoll, I was enabled to analyze 799 autopsies of children who had died at the New York Foundling Asylum, the ages varying as shown on this chart.

CHART VII.

Age Chart.

Analysis of 799 Cases. New York Foundling Asylum, 1898-1903.

Stillborn	to 3 months	. . . . .	85 cases.
3 months	to 6 "	. . . . .	140 "
6 months	to 9 "	. . . . .	155 "
9 months	to 1 year	. . . . .	140 "
1 year	to 2 years	. . . . .	141 "
2 years	to 3 "	. . . . .	87 "
3 years	to 4 "	. . . . .	37 "
4 years, 13 days			
4 years, 1 month, 10 days			
4 years, 2 months, 4 "			
4 years, 7 months, 24 "			
4 years, 8 months, 12 "			
4 years, 9 months, 6 "			
5 years, 5 days.			
5 years, 14 "			
5 years, 3 months, 18 days			
6 years, 1 month, 13 "			
7 years, 4 months, 19 "			
10 years,			

1 case each.

Result of analysis:

Arteriosclerosis	. . . . .	1 case.
Endocarditis	. . . . .	1 "
Aneurysm	. . . . .	0 "

This list comprises tuberculosis in many localities. Pneumonia, empyema, gangrene of lung, scarlet fever, meningitis (all types), septicæmia, abscesses, nephritis, besides many other conditions which have not the bearing upon arterial disease that the above have. In addition to these there were 10 cases of congenital syphilis.

In all 799 cases there occurs only 1 case of atheroma and 1 case of endocârditis. No case of aneurysm.

This 1 case of atheroma was that of a boy, aged two years, six months and six days, who died of bronchopneumonia. There was an old appendicitis, focal necrosis in the liver and "slight atheroma of the aorta." Undoubtedly a case of sepsis.

In order to determine the age at which aneurysm is the commonest, 340 autopsy reports from literature were analyzed, with results as shown on this chart.

CHART VIII.

## Aneurysm Cases from Literature.

1 to 5 years.	.	.	.	.	.	.	.	.	.	2 cases.	2½ yrs. and 5 yrs
6 " 10 "	.	.	.	.	.	.	.	.	.	3 "	
11 " 20 "	.	.	.	.	.	.	.	.	.	27 "	
21 " 30 "	.	.	.	.	.	.	.	.	.	54 "	
31 " 40 "	.	.	.	.	.	.	.	.	.	102 "	
41 " 50 "	.	.	.	.	.	.	.	.	.	90 "	
51 " 60 "	.	.	.	.	.	.	.	.	.	43 "	
61 " 70 "	.	.	.	.	.	.	.	.	.	15 "	
71 " 80 "	.	.	.	.	.	.	.	.	.	3 "	
81 " 90 "	.	.	.	.	.	.	.	.	.	0 "	
91 " 100 "	.	.	.	.	.	.	.	.	.	0 "	
										340	"

In regard to sex : of 347 autopsy analyses the following was found :

Aneurysm.	Male	.	.	.	.	.	.	.	280
	Female	.	.	.	.	.	.	.	67
Total . . . . .									347

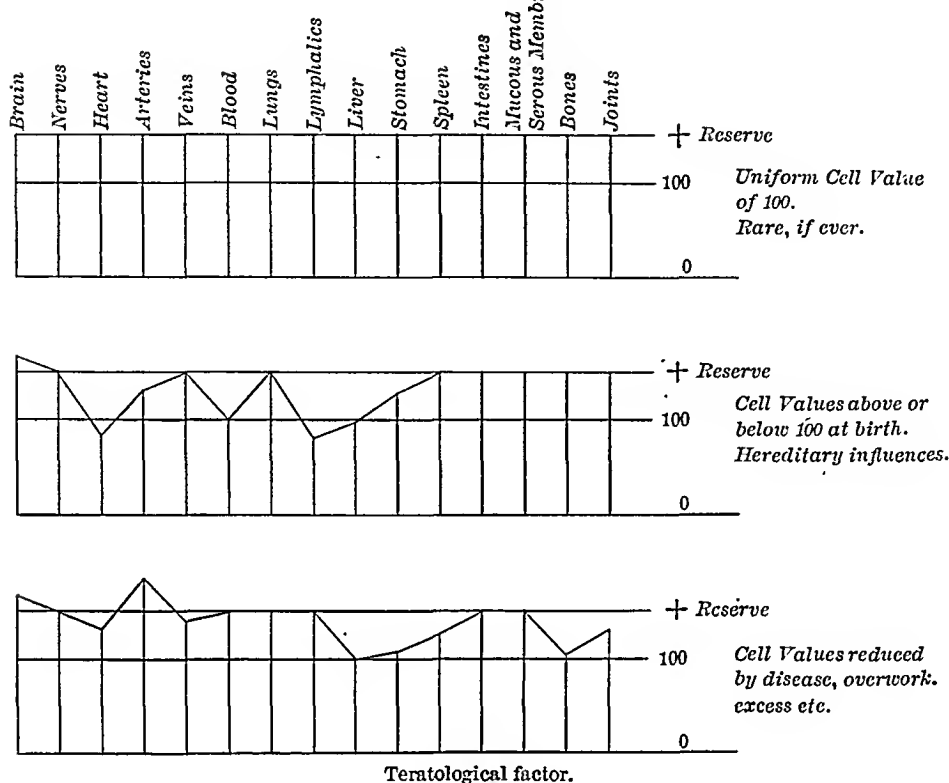
## THE TERATOLOGICAL FACTOR.

A factor in arterial disease impossible to determine experimentally, but one none the less important, is that of teratology. The various parts of the body must be considered to possess a limited degree of reconstructive power.

Regeneration must have its limit. Cells of the kidney and liver, the heart, the brain, may not all have the same reconstructive energy. They differ from one another in an individual, and they differ from each other in different individuals. This is diagrammatically shown in Chart IX.

We might then speak of the "cell equation" of an individual, by which would be meant the perfection of the synergy (*συν-ἔργον*) of that system; thus the perfectly co-operative system would have a value of 100.

CHART IX.



Individuals rarely, if ever, start with such a value. The demands during life too soon become greater on one organ than on another, so that this inequality becomes greater. A process of compensation is at work throughout the system struggling to approximate the perfect cell energy value of 100. In this work of compensation the vascular system has a great part. It, too, however, has its limitation.

#### SYPHILIS AND TUBERCULOSIS.

A question, the answer to which seems to be considerably confused, is what association is there between—

1. Aneurysm or arterial disease and syphilis; also what association there is between—
2. Aneurysm and pulmonary tuberculosis.

In the question of syphilis, for example, we find Schmidt places the figures at 29 per cent., Drummond at 100 per cent., while Gerhardt finds syphilis in 53 per cent. of the cases of aneurysm. Malmsten, on the other hand, says 80 per cent. Davidson, in the *Transactions of the Pathological Society of London*, states that in 114 autopsies he found 78 cases without syphilis, in 4 of which there was atheroma of the aorta; 28 cases with syphilis, 17 of which had

atheroma—that is, 68 per cent. without syphilis, of which 5 per cent. had “atheroma,” and 40 per cent. with syphilis, of which 60 per cent. had “atheroma.” These are widely differing figures which probably arise from the great prevalence of syphilis. Had we a specific virus or organism of syphilis, as in the case of typhoid, cause and effect could be more certainly determined. I approached the question by analyzing 370 reports of autopsies on aneurysm cases.

In 106 of these syphilis was definitely mentioned. In 34 it was present; in 72 it was absent. This gives 32 per cent., or about that of Schmidt.

It would appear from these figures that syphilis is an important but by no means essential factor, nor is it invariably followed by disease of the vessel. In this question the age at which arterial disease is found must, of course, be taken into consideration.

In this connection Allbutt says: “I am beginning to regard atheroma of the aorta in young people as strong presumptive evidence of syphilis,”<sup>1</sup> though he regards syphilitic endarteritis as a distinctive process from atheroma from other causes.

I attempted to determine, if by present improved methods of treatment of syphilis, aneurysm was less common to-day than say fifty years ago, but reliable records on this point were difficult to obtain.

In regard to pulmonary tuberculosis, in 370 autopsies on aneurysm the lungs were examined and reported on in 98; 16 of these had tuberculous involvement of the lung, or 16 per cent.

Cases of pleural adhesions were not included in this estimate.

#### ARTERIAL DISEASE IN THE COLORED RACE.

Through the courtesy of Drs. Mathias Nicoll, L. Fougères Bishop, and B. T. Tilton, I was enabled to analyze 163 autopsy reports of the Lincoln Hospital, a hospital for the colored.<sup>2</sup> I was able to compare these, through the kindness of Dr. H. A. Christian, with 1928 autopsy reports of the Boston City Hospital, a hospital for the white. The result of these analyses is as follows:

##### Lincoln Hospital (colored).

Analysis of 163 autopsies.  
8 aneurysms,  $4\frac{8}{10}$  per cent.

Thoracic,	6	} 8
Abdomen,	1	
Iliac,	1	

##### Boston City Hospital (white).

1928 cases.

36 aneurysms,  $1\frac{8}{10}$  per cent.

Professors Osler and Welch gave me the opportunity to consult the clinical and pathological records of the Johns Hopkins Hospital. In the analysis of 1800 records the following data were obtained:

<sup>1</sup> Allbutt, vol. vii. p. 309.

<sup>2</sup> While this hospital has recently admitted white patients to its wards, the records of autopsies on the colored patients only are included in the above.

Johns Hopkins Hospital.				Undetermined.	Total.
Colored wards	.	.	.	22 cases	} 7 cases. } 52 cases.
White	"	.	.	23 "	

Thus 52 aneurysms were found in 1800 autopsies. The number of white patients in this hospital outnumber the colored by about 4 to 1. These figures would indicate that aneurysm was found three or four times more frequently in the colored than in the white. Taking then the combined figures of these three large hospitals, the Lincoln, the Boston City, and the Johns Hopkins, we find aneurysm from three to four times as common in the colored as in the white.

Granting syphilis and exposure to be etiological factors, the greater frequency of aneurysm in the colored is to be expected. No reliable figures on the relative frequency of syphilis in the white and colored from which to draw conclusions on that point could be obtained.

#### ARTERIOSCLEROSIS AND ANEURYSM.

A question of great clinical value is whether general arteriosclerosis is or is not an indication of tendency to aneurysm.

This question suggested itself by the fact that cases of aneurysm of the aorta not infrequently have soft radials.

In pursuit of this point, 370 autopsy reports of aneurysm cases were analyzed, in 300 of which no reference was made to the peripheral vessels. In 70, however, the vessels were carefully examined throughout; 6 of these showed general arteriosclerosis; 64 of these showed no arteriosclerosis.

When the vasa vasora are involved first, localized softening of the media occurs with secondary changes in the intima. This weakening of the media leads to aneurysm. The intima in small aneurysms (sacculated aneurysm) we know is often not ruptured.

In arteriosclerosis, on the other hand, the intima is first involved, the media showing general loss of elasticity. General arteriosclerosis is not, therefore, necessarily associated with aneurysm.

An attempt was made to determine the relative frequency of arteriosclerosis and aneurysm in the various arteries.

Chart X. represents the result of this effort. In interpreting this chart it must be remembered that while multiple aneurysm is the exception, multiple arteriosclerosis (that is, several arteries involved at the same time) is common. Thus, of 100 sclerosed vessels, the radial will be found involved in 87 per cent., while of 100 aneurysms not one of the radial will be found.

It seems reasonable to conclude that in cases of generally thickened vessels, aneurysm is not a likely complication—*i. e.*, from the table here given it occurs in about 8 per cent.

DISTRIBUTION OF ARTERIOSCLEROSIS. The factors which determine the distribution of sclerosis of the vessels are varied. It may,

however, be stated generally that when the peripheral vessels are markedly sclerosed the abdominal vessels are free from such involvement, and *vice versa*. Great functional demand upon any part is apt to lead to sclerosis of the vessels of that organ. Thus the cerebral vessels in brain-workers are often sclerosed. The coronaries in hypertrophied heart, the radials in laborers, etc.

CHART X.

Location Chart.

	Aneurysm (from Literature).	Arteriosclerosis (Thoma and Bregmann.)
Ulnar . . . . .	$\frac{1}{2}$ per cent.	94 per cent.
Anterior tibial . . . . .	$\frac{1}{4}$ "	93 "
Subclavian . . . . .	5 "	88 "
Cerebral { anterior, middle, poste- rior, ant. common, post. common, basilar, and mid. meningeal }	8 "	87 "
Internal carotid . . . . .	1 "	87 "
Radial . . . . .	0 "	86 "
Splenic . . . . .	1 "	82 "
Popliteal . . . . .	14 "	79 "
External carotid . . . . .	$\frac{1}{4}$ "	78 "
Axillary . . . . .	1 "	71 "
Femoral . . . . .	5 "	69 "
Common carotid . . . . .	1 "	68 "
Ascending aorta . . . . .	34 "	67 "
Abdominal aorta . . . . .	8 "	64 "
External iliac . . . . .	1 "	58 "
Brachial . . . . .	2 "	55 "
Common iliac . . . . .	1 "	
Innominate . . . . .	3 "	
Thyroid axis . . . . .	$\frac{1}{4}$ "	
Pulmonary . . . . .	3 "	
Coronary . . . . .	1 "	
Cœliac axis . . . . .	$\frac{1}{4}$ "	
Sylvian . . . . .	$\frac{1}{4}$ "	
Basilic . . . . .	$\frac{1}{4}$ "	
Hepatic . . . . .	2 "	
Plantar . . . . .	$\frac{1}{2}$ "	
Profunda . . . . .	$\frac{1}{4}$ "	
Superior mesenteric . . . . .	1 "	
Pons varolii . . . . .	$\frac{1}{4}$ "	

PHYSICAL PROPERTY OF ARTERIES.

What, now, are the properties of this wall whose chief element in construction is elastic tissue? The analogy between the elasticity of vessels and other elastic bodies at once suggests itself. It is found, however, by Wertheim and Weber, that the laws governing the elasticity of organized bodies, such as the vessel wall, differ from unorganized bodies, such as rubber. This difference is put down to the intrinsic moisture of organized bodies.

We have then to consider the organized structure apart from the unorganized, and must take into account four properties: elasticity, resiliency, extensibility, and resistance.



The elasticity of a substance refers (1) both to its ability to resist deformation and (2) to its ability after deformation to resume its original shape. These two ideas may be conveniently combined by supposing that no force is applied sufficient to permanently deform the object tested. Supposition number two above is, therefore, always understood to control the test; that is, that the object is not permanently deformed by the test.

The force at which permanent deformation occurs is the limit of the forces producing temporary only deformation, and this force is called the *elastic limit*.

For example, suppose that we stretch a wire or a rubber band a little, and then relax the stress. The elongation produced at first disappears when the stress is relaxed. We say that the recoil is equal to the elongation. Suppose that we then continue this process of alternately pulling and relaxing, measuring the elongations and the recoils, and increasing the pull every time. Up to a certain pull, or tensile stress, we find the recoils always equal to the preceding elongations; that is, that the deformation produced by the pull is not permanent.

After this limit (the elastic limit) has been passed we find the recoils are not as great as the preceding elongations, or that the object has stretched.

As a rule, the usefulness of anything that is permanently stretched is gone, therefore we study the properties of materials only below the elastic limit. These properties are the elastic properties.

The main elastic properties are:

1. The value of the elastic limit—*e. g.*, the pull in pounds per square inch that will permanently stretch the object. This has been defined above.

2. The rate at which the object stretches; that is, the extent of its elongation for a given pull. In a spiral spring this might be called the stiffness of the spring. Scientifically this is called the coefficient or modulus of the object's elasticity. This is a long and often confusing term, but the real idea it expresses is a very simple one. It is an application of the principle that "science is measurement." In other words, the coefficient is a numerical term by which the stiffness of objects may be compared; that is, of two objects stretching unequally under a given pull, the stiffest is that which stretches *least*. But if we measured the elasticity (that is, the coefficient of elasticity) by the stretch alone, the stiffest object would have the least numerical expression for its coefficient, which would be confusing.

For example: The spiral spring *A* under a pull of 100 pounds stretches one inch. The spiral spring *B* under a pull of 100 pounds stretches two inches. It is evident that *A* is the stiffer of the two springs, and that its coefficient is double that of *B*, yet its stretch is only one-half as much. So we say that the coefficient is measured

by the pull divided by the stretch. Thus the coefficient of spring *A* is 100 pounds, and the coefficient of spring *B* is fifty pounds.

NOTE.—It is assumed that all other circumstances of the experiment are identical in the two objects *A* and *B*. It is apparent that while *A* is stiffer than *B*, yet it may be made, say of a different metal, so that *B* may have a higher elastic limit, although its coefficient may be lower.

Chart XI., Figs. 1 and 2, presents simple diagrams which will illustrate this.

Suppose that a pull of 100 pounds elongates the spring one-half inch with a recoil of the same extent. In the diagram Fig. 1 we illustrate this by the dot *a*. Similarly we find *b* and *c*. But when we make the pull 400 pounds we get the dot *d* with a recoil from *d* to the one-and-a-half-inch mark.

Let us join the points by a line as in Fig. 2. Then this line expresses all the elasticity characteristics of the object tested. The elastic limit is 300 pounds, for after this pull the extensions increase more rapidly than the recoils, or the spring has been permanently stretched—*e. g.*, two inches from 0 to 2. The back of the curve, like that of the resistance of the spring is broken at the “hump.”

Chart XI., Figs. 3 and 4, shows another diagram containing the above figures, and the similar “strain diagram” of another spring.

In this case (Fig. 3), as in the hypothetical case, *A* is stiffer (or has a higher coefficient) than *B*, yet its elastic limit is only two-thirds that of *B*.

These diagrams represent the behavior of unorganized bodies. Let us now see how organized bodies behave under similar treatment.

As a rule, the strain-diagram shows a straight line below the elastic limit; that is, for the portion of it from 0 to the “hump,” so that the elasticity of the springs *A* and *B* may be compared by dividing the one pull—200 pounds which they have in common below the elastic limit—by the corresponding extensions, *viz.*, one-half inch for *A* and one inch for *B*, making *A* twice as stiff (or elastic) as *B*, as before assumed. In these cases the coefficient for each spring is constant, though the different springs have different coefficients. Sometimes, however, the strain diagram is represented by a curve, as in Fig. 4. In this case we suppose that the curve is straight at the point in question as at *a*, *b*, *c*, or *d*. At these points draw tangents to the curve. We then compare the inclinations of the tangents. In this case the curve *C* shows that the stiffness is diminishing, and in curve *D* that it is increasing.

This latter increasing coefficient expresses the behavior of the artery as distinguished from the decreasing coefficient of unorganized bodies.

These diagrams are not fanciful, for the specimen may be made to write them autographically.

CHART XI.

FIG. 1.

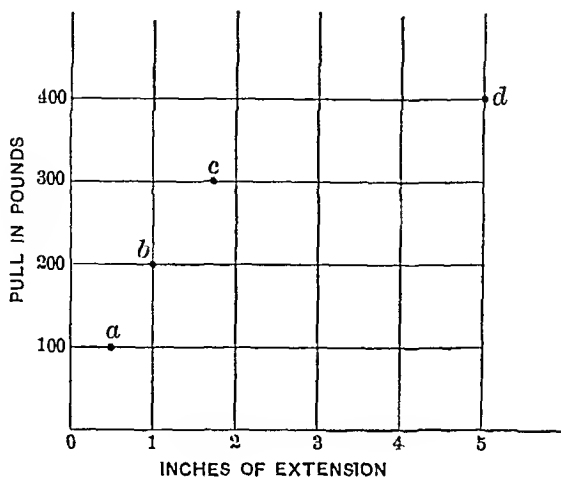


FIG. 2.

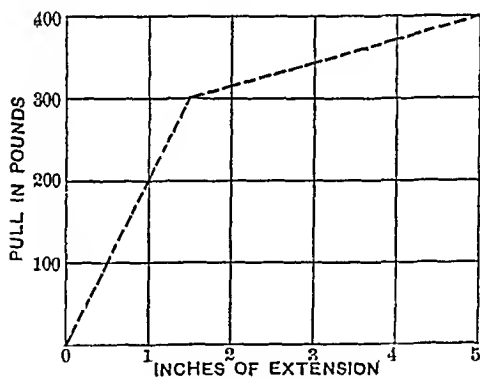


FIG. 3.

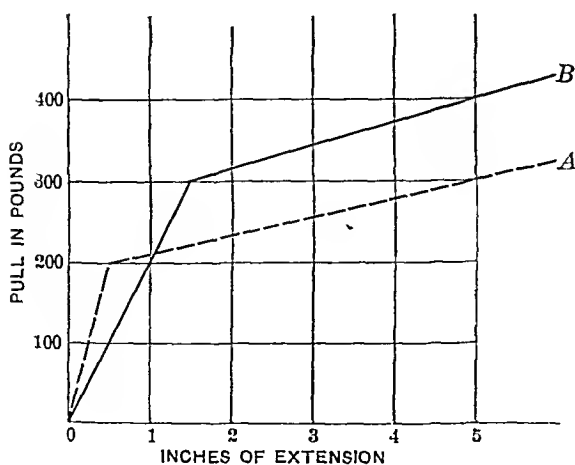
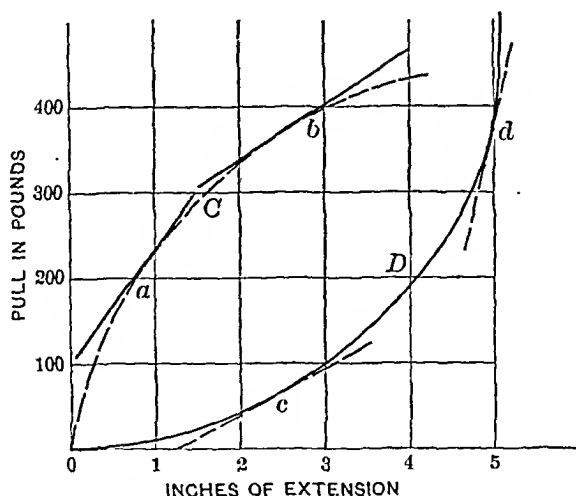


FIG. 4.



Coefficient of elasticity of organized as compared with unorganized bodies.

The elasticity of various organized substances is shown in Chart XII., also the relative elasticity of normal and diseased arteries.

CHART XII.

Relative elasticity of various tissues. (From Schäfer.)

Bones, dried . . . . .	Similar to inorganic bodies.
Sinews, dried . . . . .	Similar to fresh bone.
Nerves, dried . . . . .	Similar to fresh sinew.
Muscles.	
Arteries.	

Relative elasticity of normal and diseased arteries:

Normal.	Weight, 100 grm.	Sclerosed.
Stretched.	Length.	Stretched.
16.5 cm.	7.5 cm.	9.9 cm.
Recovery:		Recovery:
8 cm.		8 cm.

Elasticity and resiliency diminished, especially elasticity.

To attain the greatest strength with a given amount of material, a cylinder should be constructed of layers, the elastic coefficient of which gradually increases from within outward. Now, this is exactly the arrangement of the different layers of the arterial wall; thus the greatest strength is attained by the smallest amount of material consistent with safety. Similar reasoning applies to the walls of a sphere, to which an aneurysm is comparable, from which it appears the main source of weakness in an aneurysm is, that the wall practically is composed of only one coat (Nicolls and Schäfer, p. 74). The human artery from this arrangement is physically perfect for the demands made upon it. This adaptability is demonstrated in Chart XI., Fig. 4, in which, according to Wertheim (as quoted by Schäfer, p. 72), the coefficient of elasticity of an excised strip of an artery is not constant but *with the extension increases*.

This property of increased coefficient of elasticity leads to a storing up of intermittent energy of the heart (Nicolls and Schäfer), which, if lost by disease, must greatly influence the rate of flow and thus furnish one of Thoma's essential factors in intima change.

In this connection, Dr. George McClellan calls my attention to an important anatomical fact, namely, the attachments of the great vessels to the deep cervical fascia, rendering them less movable, a fact which may be one reason why the arch of the aorta is so much more commonly affected than other arteries.

Very thorough investigation upon these physical properties of the arterial wall, together with histological observation upon the vessels experimented upon was carried out by August Luck in 1889, under the supervision of Prof. Thoma.

This work went to show that the normal artery has a greater resiliency than elasticity, while the reverse is true of the sclerosed vessel. In the initial stage of arteriosclerosis, that is, just before the thickening of the intima began, the vessel was found to be more expansile, but the elasticity was diminished. This change was found in vessels in which, histologically, no abnormal tissue could be detected.

#### CHART XIII.

##### Breaking strain of arteries.

(From various sources, together with personal observation.)

I. Normal vessels.	Pressures.
Carotid of goat.	2250 mm. Hg. 14 times the normal.
Carotid of dog.	3000 to 8500 mm. Hg.
Carotid of dog injured, intima and media slightly damaged.	At 450 mm. a pouch formed, but vessel did not rupture.
Human carotid.	1290 mm. Hg.
Large arteries rupture at lower tension than small arteries.	
II. Diseased.	
Localized sclerosis.	280 to 300 mm.-Hg. Intima and media burst. Mercury trickled through adventitia.
Atheromatous plaques.	150 mm. Hg.
Generally thickened vessels.	1200 mm. Hg.

##### Breaking strain of veins.

Higher pressure required to rupture corresponding veins.

I am engaged in experiments along this line which seems a neglected but very important branch of the subject.

I am indebted to Captain Metcalfe, U. S. A., retired, and formerly instructor in ordnance and gunnery at West Point, for practical suggestions in the construction of apparatus to test the physical properties of arteries and for the explanation of the physical properties of unorganized substances.

#### HISTOLOGICAL PROPERTY OF ARTERIES.

All the evidence at hand goes to show that the seat of the most important change is the elastic tissue of the media. What is the nature of this change? It may be molecular, that is, purely physical; or it may be histological, that is, some tissue change. If the former, it can be detected only through changes in the physical properties

of the artery and microscopic appearances characteristic of molecular change in the elastic contents. If the latter, that is, histological, we should be able to detect this through staining and chemical peculiarities. That the diseased artery shows marked variation from the normal in its physical properties, the facts just stated, together with evidence not here quoted, goes to show. The question then is, are there histological changes as well, or is it solely a molecular or physical change?

Attention was therefore directed to the microscopic appearance of the elastic tissue.

Thirty-three human arteries, consisting of the aorta, the popliteal, and coronary were subjected to stains selective of the elastic tissue. These vessels were both normal and diseased—the latter being composed of all stages of sclerosis to actual aneurysm formation. About 150 sections were thus treated and compared.

The stains employed were:

1. The Weigert.
2. The Unna Taenzer.
3. The Mallory.

4. Eosin hæmatoxylin stain was employed when information upon the vasa vasora was desired.

Each specimen was stained by all of these methods, so that they present a thorough demonstration of the relative merits of each method. A great variety of fixation agents was employed and experimented with. The best fixation agent is the Müller formalin, and the best stain the Weigert.

The steps in the staining are here briefly given.

**TECHNIQUE EMPLOYED IN STAINING ELASTIC TISSUE.** After experimenting with the various fixatives and hardening agents, as well as the different methods given in works on pathological technique for staining elastic fibres, it was found that the following gave best results:

1. *Weigert's Method* (Fig. 1). *Centralblatt für Allgemeine Path. u. Path. Anatomie*, May, 1898, vol. ix. p. 289.

Tissue stained equally well when fixed and hardened in Müller, formol or Müller-formol.

Formula is:

Fuchsin (not Rubin S)	1 per cent.
Resorcin	2 "
Water	200 c.c.

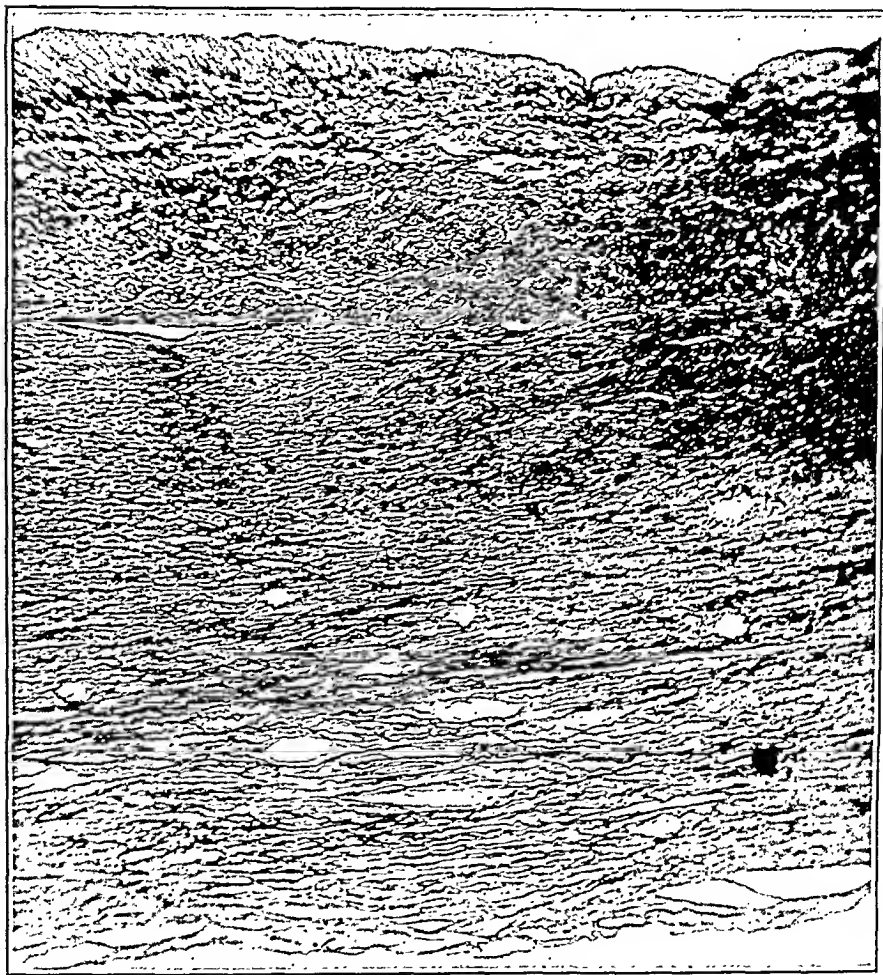
Boil in a porcelain capsule. When boiling add 25 c.c. liq. ferri sesquichlorati (Ph. G. III.), and boil 2 to 5 minutes longer, stirring meanwhile. Cool and filter.

Throw away filtrate. When precipitate is dry, place it in same capsule and add 200 c.c. 94 per cent. alcohol. Stir and let it boil, fishing out the pieces of paper. Then cool, filter, and to filtrate add enough 94 per cent. alcohol to make 200 c.c. Lastly add 4 c.c. HCl.

Stain may be used repeatedly.

For the present work, tissue was embedded in paraffin and sections cut 8 to 10 $\mu$ . It was found that the best stains were obtained in ten to fifteen minutes instead of twenty minutes to one hour, as advised by Weigert, then washed in 95 per cent. alcohol, left for a few seconds in 100 per cent., cleared in xylol and mounted

FIG. 1.



Selective elastic-tissue staining.  $\times 160$ . Aorta (human). Weigert. See text, p. 865. Note that the darker area in the middle of the section is due to a folding of the tissue and not to any histological change. (From the Cornell University Photomicrographic Laboratory, N. Y.)

in balsam. If overstained, acidulated alcohol hastens removal of excess.

Elastic fibres are dark blue against a pale or colorless background.

## II. *Unna Taenzer, modified* (Fig. 2).

Müller, formol, Müller-formol, alcohol, and bichloride may be used for this method.

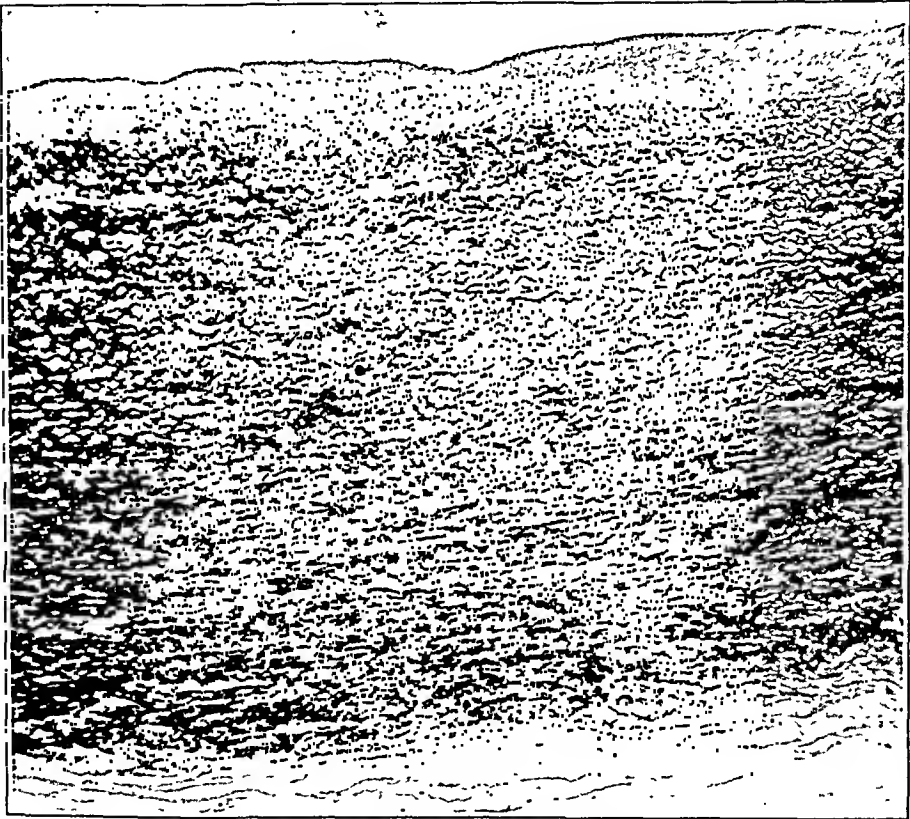
Formula for stain is:

Orcein (Grübler) . . . . .	0.59 gm.
Absolute alcohol . . . . .	40 c.c.
Distilled water . . . . .	20 "
HCl . . . . .	15 to 20 gtt.

Allow section to remain in this overnight, or about fifteen hours, then differentiate in:

Alcohol (95 per cent.) . . . . .	20 c.c.
Distilled water . . . . .	5 "
HCl . . . . .	1 to 2 gtt.

Fig. 2.



Selective elastic-tissue staining.  $\times 185$ . Unna Taenzer. See text, p. 866. (From the Cornell University Photomicrographic Laboratory, N. Y.)

Pass through absolute alcohol and mount in Canada balsam. Elastic fibres are brown against a very pale or colorless background.

III. Mallory (Mallory and Wright's *Path. Technic*, p. 243, ed. 1897.)

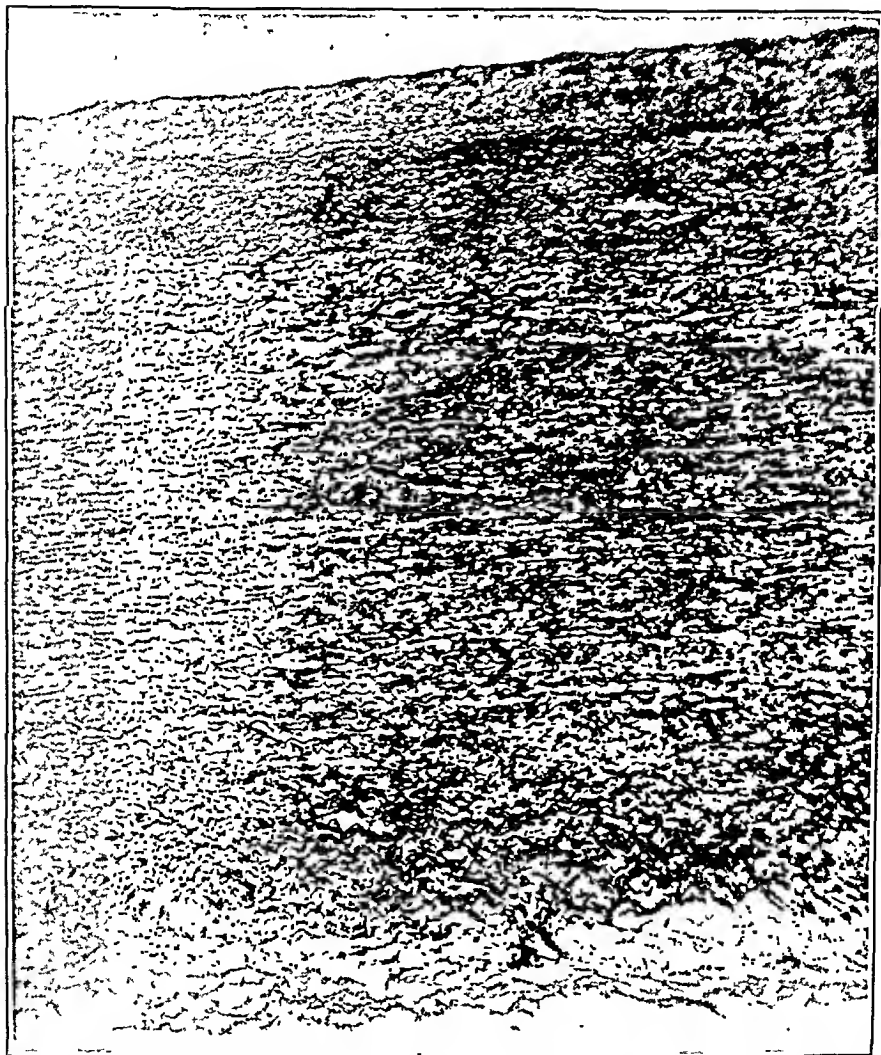
Alcohol is the best hardening agent, a point emphasized by Mallory.

Phosphotungstic acid (1 per cent. aq. sol.) . . . . .	100 c.c.
Hæmatoxylin . . . . .	1 gm.



Sections are allowed to remain in stain overnight, washed in 95 per cent. alcohol, then 100 per cent., cleared in xylol and mounted in Canada balsam. If overstained acidulated alcohol will remove the excess. Fibres are a decided blue in a very pale pink background.

FIG. 3.



Tissue digestion experiments. Slightly sclerosed.  $\times 160$ . Section of aorta (human) treated with 1 per cent. acetic acid. Stained with elastic-tissue selective stain. No change in tissue noted. See text, p. 867. (From the Cornell University Photomicrographic Laboratory, N. Y.)

The specimens, photomicrographs of which are here given (Figs. 1 and 2), show the following:

1. Vessels which in the gross display no signs of sclerotic change may, under the microscope, show slight thickening of the intima.

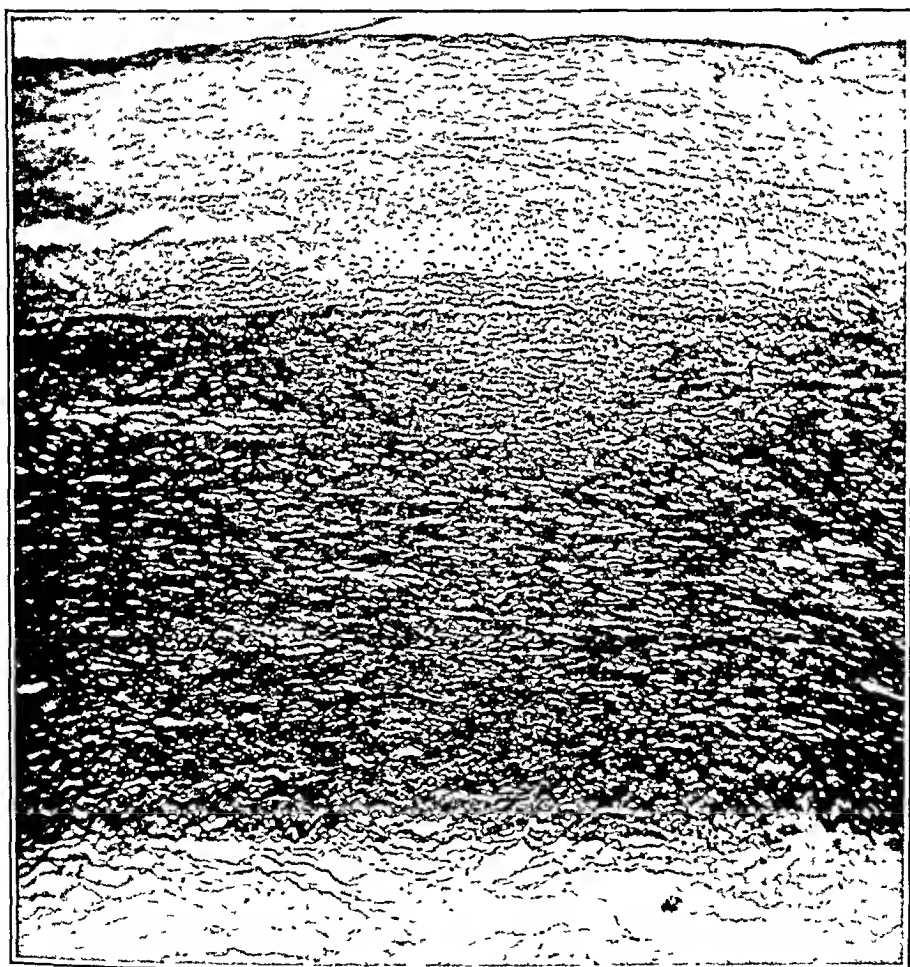
2. The elastic tissue shows the corkscrew character modified—the strands being straighter, more separated from one another, and in some instances fewer.

These then are probably mechanical changes, the stains failing to demonstrate any histological change in the elastic tissue.

#### DIGESTION EXPERIMENTS.

The next set of experiments was of a chemical nature, dealing with the reaction of the elastic tissue to digestants.

FIG. 4.



Tissue digestion experiments.  $\times 185$ . More advanced sclerosis than preceding. Section of aorta (human) treated with 1 per cent. acetic acid. Stained with elastic-tissue selective stain. No change in tissue noted. See text, p. 866. (From the Cornell University Photomicrographic Laboratory, N. Y.)

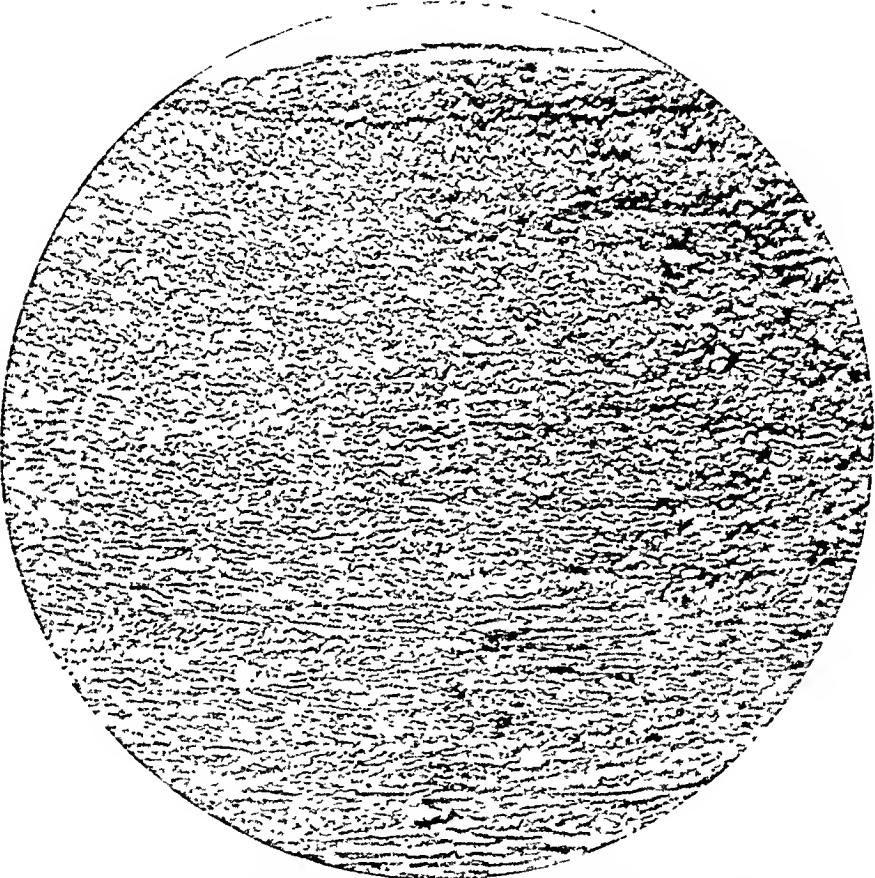
The object of this work was to demonstrate, if possible, through the action of digestants whether the change which takes place in the elastic tissue is of an histological or physical character.

The following experiments were therefore taken up. The digestants selected were acetic acid and potassium hydroxide.

*Technique in the Attempt to Digest Elastic Tissue in Arteries with Acetic Acid and Potassium Hydroxide.*

1. An aorta *hardened for several weeks* in Müller's fluid was chosen, and the area showing arteriosclerosis was subjected to the acid and alkali, as follows:

FIG. 5.



Tissue digestion experiments.  $\times 185$ . Slightly sclerosed. Section of aorta (human) treated with 5 per cent. acetic acid. Stained with elastic-tissue selective stain. No change in tissue noted. See text, p. 866.

(a) *Acetic Acid.* 1. Strength of 1, 2, 3, 4, 5, 10 and 20 per cent. *acetic acid* were allowed to act in the incubator for twenty-four hours. Tissue being macroscopically unchanged, it was washed in running water for twenty-four hours.

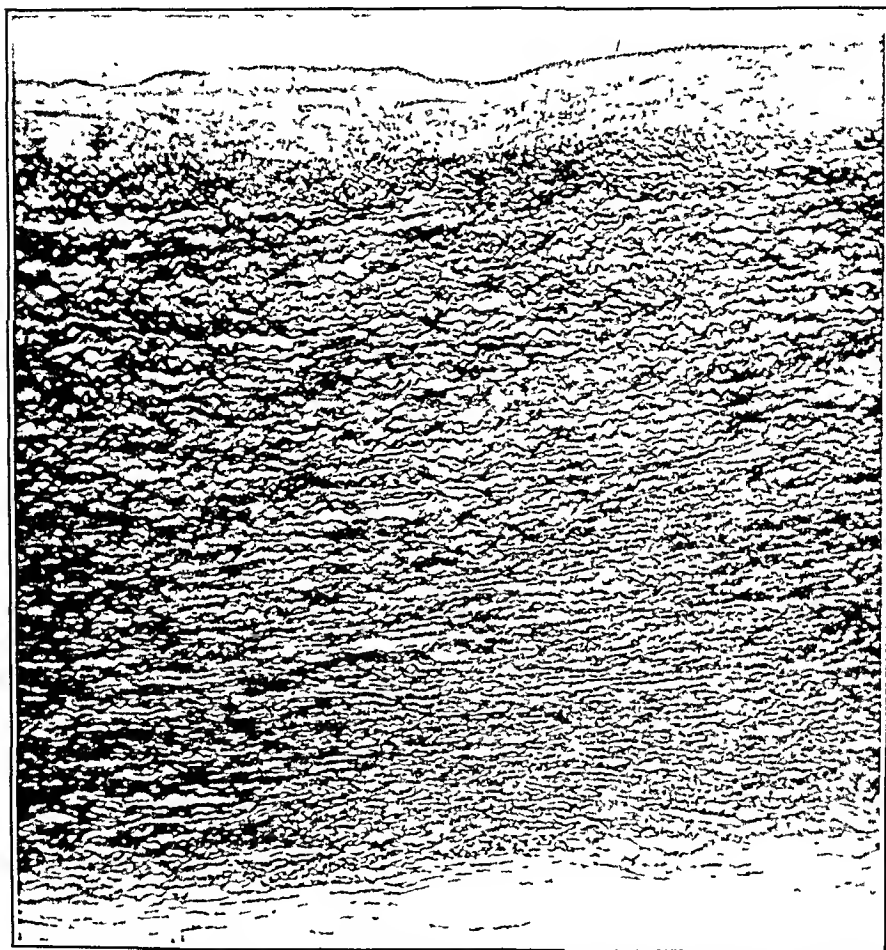
Dehydrated in

95 per cent. alcohol in incubator	.	.	.	.	.	24 hours.
100 " " " "	.	.	.	.	.	48 " (changed once).
Anilin oil " "	.	.	.	.	.	overnight.
Xylol " "	.	.	.	.	.	24 hours.
" paraffin " "	.	.	.	.	.	24 "
Soft " in oven . . .	.	.	.	.	.	24 "
Hard " " . . . . .	.	.	.	.	.	24 " and then embedded.

2. Specimens treated with same strength at room temperature for twenty-four hours appeared unaffected and were put through as preceding.

3. Another set of specimens were subjected to the same strengths of the acid for seventy-two hours at room temperature and no

FIG. 6.



Tissue digestion experiments.  $\times 185$ . More advanced sclerosis than preceding. Section of aorta (human) treated with 5 per cent. acetic acid. Stained with elastic-tissue selective stain. No change in tissue noted. See text, p. 870 (From the Cornell University Photomicrographic Laboratory, N. Y.)

apparent change. Further treatment was the same as preceding. (Figs. 3, 4, 5, and 6.)

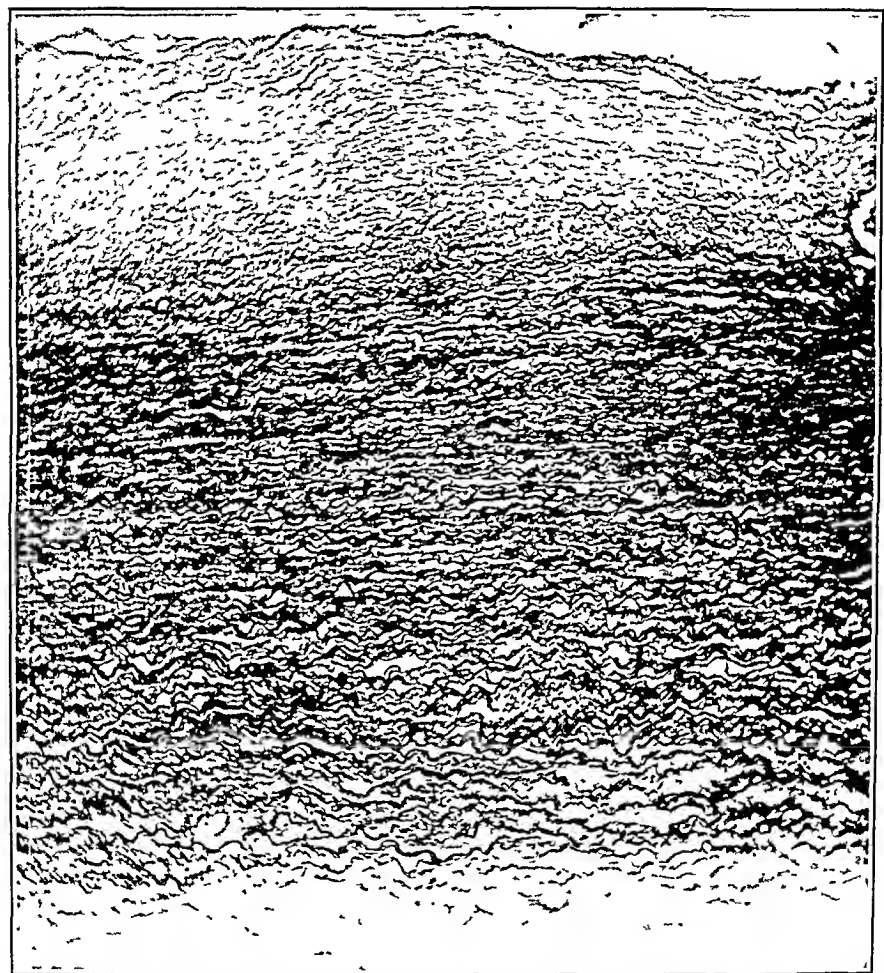
(b) *Potassium hydroxide*, KOH, 5, 10 and 20 per cent., in incubator for twenty-four hours, dissolved the tissue.

At room temperature for twenty-four hours, 10 and 20 per cent. partially disintegrated; 5 per cent. was left soft but intact; latter washed in running water for two hours.

Tissues were disintegrated. The strengths 5 per cent. and above are, therefore, not practical. (Figs. 7 and 8.)

Fresh material with marked arteriosclerosis was selected for another trial.

FIG. 7.



Tissue digestion experiments.  $\times 185$  Section of aorta (human) treated with 1 per cent. KOH. Stained with elastic-tissue selective stain. No change in tissue noted. See text, p. 871. (From the Cornell University Photomicrographic Laboratory, N. Y.)

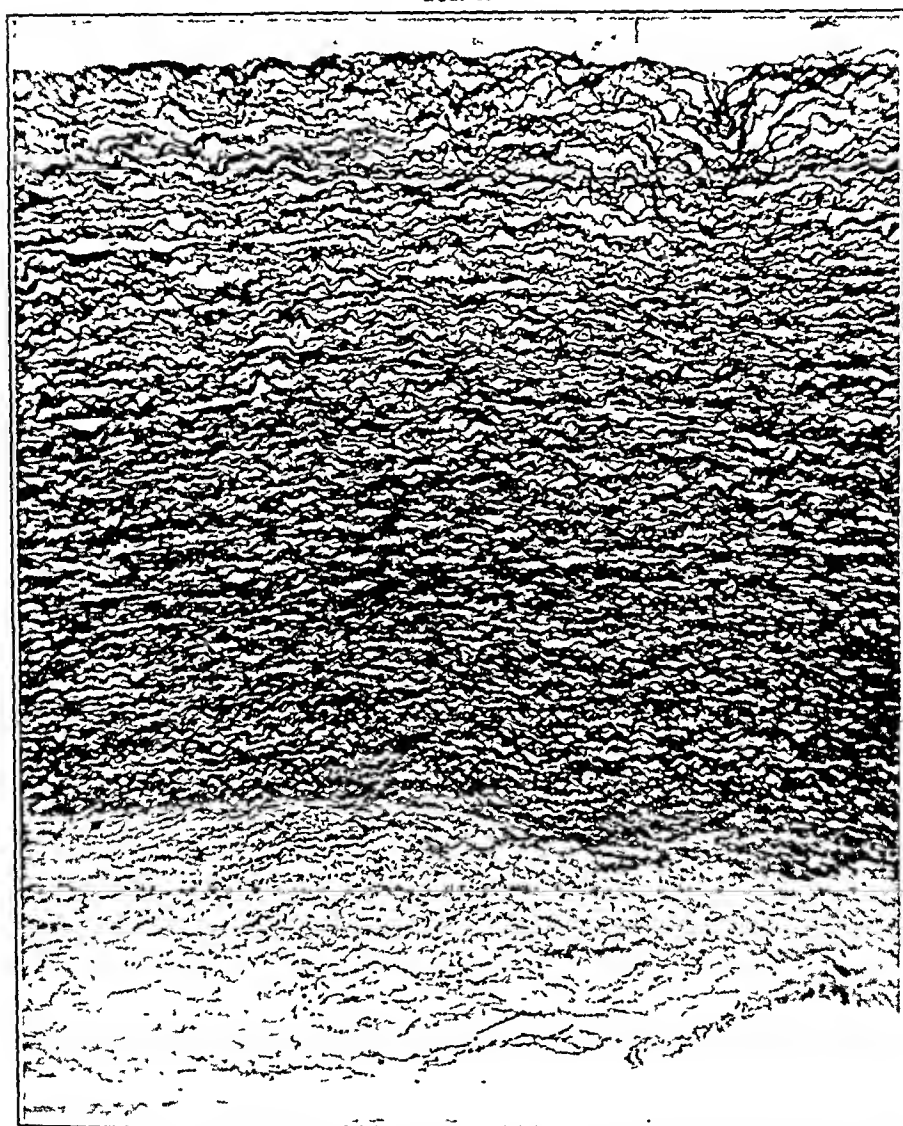
(a) 1. *Acetic acid*, 5, 10 and 20 per cent., in incubator twenty-four hours. Tissue softened.

80 per cent. alcohol, room temperature	.	.	.	.	24 hours.	
95 " " " "	.	.	.	.	24 "	
100 " " " "	.	.	.	.	24 "	
95 " " " "	.	.	.	.	24 "	
80 " " " "	.	.	.	.	24 "	
Running water	.	.	.	.	24 "	
80 per cent. alcohol in incubator	.	.	.	.	24 "	
95 " " " "	.	.	.	.	24 "	
100 " " " "	.	.	.	.	48 "	(changed once).
Amlin oil	.	.	.	.	24 "	
Xylol	.	.	.	.	24 "	
" paraffin	.	.	.	.	24 "	
Soft " in oven	.	.	.	.	24 "	
Hard " "	.	.	.	.	24 "	(embedded).

2. *Acetic acid*, 5, 10 and 20 per cent., at room temperature for twenty-four hours. Tissue quite firm and treated as above.

(b) *Potassium Hydroxide*. 1. KOH, 1, 2, 3, 4, 5, 10, 15 and 20 per cent. in incubator twenty-four hours; 5, 10 and 20 per cent. completely disintegrated; 4 per cent. partially broken up and fell

FIG. 8.



Tissue digestion experiments.  $\times 185$ . Section of aorta (human) treated with 2 per cent. KOH. Stained with elastic-tissue selective stain. No change in tissue noted. See text, p. 871. (From the Cornell University Photomicrographic Laboratory, N. Y.)

to pieces in transferring to alcohol; 3 per cent. very soft but intact; 1 per cent. and 2 per cent. fairly firm. Last three put through same process as II. a.

2. KOH, 1, 2, 3, 4, 5, 10, 15 and 20 per cent. at room temperature for twenty-four hours; 10 and 20 per cent. dissolved; 5, 4

and 3 per cent., very much softened, 2 and 1 per cent. less so, but carried through the different grades of alcohol and media as preceding.

CONCLUSION. The elastic tissue having resisted the digesting agent is probably not the seat of any histological change. It has probably undergone a molecular or physical change.

Selective stains and digesting agents failing to detect any histological change leave the molecular change theory while not proven yet with points in its favor. - It leaves, however, the question of vasa vasora change untouched. To this source for early nutritive changes one inevitably comes, though it cannot in all cases be shown. This question is not given such slight reference with any disregard to its importance, but the search was on other lines, and the changes in the vascular supply to the vessels is mentioned here that it may not be thought to have been overlooked.

These experiments, as far as I know, have not before been attempted. Mall's experiments in digesting, with running water, all the substances of an organ leaving only the trabeculæ are of another nature. I regret that a greater number of specimens was not subjected to these experiments, but the specimens, photomicrographs of a few of which are here presented, required many months in the preparing, as the methods are long and tedious and the material could only be of the freshest, Museum specimens being out of the question.

The work is published not as a demonstration of any important conclusion, but merely as a suggestion which may yield better results to workers in the field of physiological chemistry.

#### CONCLUSION.

To sum up the findings then:

1. Arterial disease appears to be rare, almost unknown in animals. Syphilis being probably peculiar to man is by this observation placed more firmly in the list of etiological factors.

2. Arterial disease in children under six years, even in those who are victims of congenital syphilis, is practically unknown. In those from six to fifteen years it is rare. It is found in the initial stage most commonly between the ages of thirty and forty years.

3. The teratologic factor, though an undeterminable one, is of great importance.

4. Arterial disease seems to be attributable to syphilis in about 32 per cent.; to tuberculosis in about 16 per cent.

5. The facts presented go to show that the colored race is affected about four times more frequently than the white.

6. General arteriosclerosis seems to be not commonly found with aneurysm and its presence may be considered as evidence against the probable development of aneurysm.



7. Staining with selective stains and treating with a chemical which digests tissue shows the elastic tissue to be free of histological alterations, suggesting that this tissue undergoes physical or molecular rather than histological change.

To Dr. Jagle, who assisted me in the histological and digesting work, I want to express my appreciation of the patience and thoroughness displayed throughout, but especially at times discouraging to us both. Also to Dr. McClellan and Professor Ewing I am indebted for valuable suggestions. From Dr. Elser I obtained practical aid in the digestion experiments, and Dr. George Warren rendered me assistance in examination of autopsy records, without which much of the material here presented could not have been collected. To Dr. Schoenberg I am indebted for aid in collecting the foreign literature.

I wish to express my appreciation of the opportunity given me by the committee of the Mütter Museum to present this report, trusting that the observations may prove of value to the practitioner and offer suggestions to those who have the opportunity of the laboratory in which to work out these problems.

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## REPORT OF A CASE OF LAMINECTOMY FOR GUNSHOT WOUND OF THE SPINE.

BY JAMES P. MARSH, M.D.,

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W. M. entered my service at the Samaritan Hospital August 11, 1903. He is a farmer by occupation, twenty-five years of age, white, born in the United States, and married.

He complains of severe pain at the lower part of the thorax, which extends around the body, and has some of the characteristics of a "girdle sensation." He also complains of nearly complete paralysis of his legs, especially of the left one.

The patient's father is alive and well, but his mother died of consumption. He has one sister who is alive and well, and one sister who died of la grippe.

W. M. says that he has never been ill or met with any accident excepting the one in question.

On June 14, 1903, he received a shot from a revolver just below and internal to the angle of the left scapula. The calibre of the bullet was 32. He immediately fell to the ground and could not move his legs at all for two weeks thereafter, and the bowel and bladder were also paralyzed. The wound bled but little and he at once experienced severe pain around the lower part of the thorax.



This pain has continued more or less until the present time. At the end of two weeks he began gradually to recover the use of his legs, the right one gaining more rapidly than the left. This improvement has continued up to the present, so that he can now stand erect and can move around a little by shoving one foot at a time across the floor.

This patient is well nourished and has a good muscular development. He has a recent scar just below and internal to the angle of the left scapula. Examination of the lungs, throat, heart, arteries, liver, and spleen is normal. Examination of the abdomen, kidneys, genital organs, mental condition, and cranial veins is negative. Both legs are diminished in muscular power, and the left one seems to be stiff, so that the patient does not have as good use of it as he does of the right one.

*Diagnosis.* Probable gunshot wound of the spine. On August 18th I took a radiograph of the spine. This showed a bullet lodged apparently in the spine on a level with the body of the eighth dorsal vertebra and a little to the left of the spinal canal.

On August 20th, he was examined by Dr. H. J. White and myself and the following notes were made: "The left pupil is larger than the right one, but both react to light and in accommodation. The tongue protrudes straight. There is no anæsthesia upon the face or neck. No jaw-jerk is present. Sensation to touch and pain upon the arms and upper portions of the thorax is normal; on the legs sensation to touch and pain is somewhat delayed, especially upon the right one. Thermic sensation is normal excepting upon the right leg, where it is somewhat confused. Analgesia is present upon the outer side of the right leg. Distinct ankle clonus is present at both ankles, and the tendon jerks are increased on both sides. There is weakness of the flexor muscles of both legs, but most marked on the left side. There is a transverse area of slight anæsthesia at the level of the twelfth dorsal and first lumbar vertebræ. A slight Babinski exists and there is patellar clonus on both sides, most marked on the right side. The plantar reflex is absent; a marked diminution in the power of the left leg is noticed and the Achilles jerk is present on both sides. In walking the feet are shoved along the floor, first one and then the other, just a little distance at a time, the left limb being very spastic and jerky."

It seemed to us that the cord had been and possibly was still pressed upon by either the bullet or a displaced portion of bone, and that an operation was indicated. Accordingly, I asked Drs. E. D. Ferguson and H. C. Gordinier to see the case in consultation with me. On August 21 Dr. Gordinier gave the patient a very careful examination and has kindly furnished me with a copy of his notes made at that time, and which are as follows: "The patient is well built and of fine musculature. There is no atrophy present. There is a rhythmic clonus of the anterior muscles of the thighs,

especially on the left side, where it involves also the calf muscles. When the patient is recumbent the feet are overextended. The patient can move the toes of each foot well, but those of the right foot more. All movements of the left leg are weak and abduction is limited, while the movements of the right leg are normal. The left leg is in slight tonic spasm. The patient cannot overcome the ordinary pressure of the hand in extending the left leg upon the thigh. The right leg equals normal. There is ataxia of the left leg; the right one equals normal; and there is no loss of muscular tone in the feet. A marked extensor spasm of the left leg occurs at intervals. Ankle clonus exists on both sides; the patellar tendon reflex is increased on both sides, but more so on the left side. There is marked patellar clonus on both sides, the left being most marked. Babinski's reflex is found on both sides, but more marked on the left. The Achilles tendon reflex is greatly exaggerated on both sides. There is slight tactile anæsthesia, to cotton, over the plantar surface of the right foot, with a strip of incomplete analgesia from the ankle along outer surface of the leg to the head of the fibula. There is no analgesia on the left leg. The temperature sense throughout the body is normal excepting for a strip on the outer side of the right leg and thigh. The umbilical reflex is absent, and there is no epigastric reflex. There are no anæsthetic areas over the anterior surface of the body. He is unable to differentiate hot and cold on the ventral surface of the right leg, ice-cold test-tubes being called warm. The upper part of the body is normal."

The eyes were examined by Dr. F. A. Smith, and he pronounced them to be normal. The urine was found to be normal.

On August 29th I made a dorsal median incision extending from the fourth dorsal to the first lumbar vertebral spines, and removed the spines and posterior arches of the seventh, eighth, and ninth dorsal vertebræ. The dura of the cord was incised for about two-and-one-half inches, and the cord appeared to be normal. Where the posterior arch of the eighth dorsal vertebra joins the transverse process on the left side was found the track of the bullet. It had not entered the spinal canal but in its passage it had forced the bone inward, so that at this point pressure had been made against the membranes of the cord. This point of protrusion into the lumen of the canal was removed. The bullet had evidently passed forward into the body of the vertebra and it did not seem wise to make further search for it. The dura was carefully sutured with tendon, the muscles were closed in layers over a small gauze drain, and the wound in the skin was closed with silk.

The pulse before anæsthesia was 90, and afterward 108. The time of anæsthesia was two hours and five minutes, the anæsthetic being at first A. C. E. mixture, followed by ether. The time of operation was one hour and fifty minutes. After the operation his temperature went as high as 101°, and his pulse varied from 130

to 60, the low point being reached on the eleventh day. The wound healed by first intention throughout, although for several days there was considerable oozing of cerebrospinal fluid from the point where the drain was removed.

On September 13th the following note was made: "Tactile sensation is greatly improved, the ankle clonus diminished, Babinski slight, ataxia in limbs improved, thermic sensations still somewhat perverted, and the muscular power in the lower limbs is stronger." On September 15th the patient was allowed to sit up in a chair and was permitted to take a few steps.

The following note was made on September 17th: "Tactile sensation is normal in the lower left limb. Just above the right ankle he is able to distinguish the dull from the sharp point. Babinski slight, lower limbs slightly ataxic, and muscular power improved. The patient can walk much better and can go up stairs much more easily than before the operation. Thermic sensation still perverted. Normal reaction to the faradic current and negative with the galvanic current."

About September 7th, the wound was found to be completely healed, but there was a very large soft swelling beneath it, which was thought to be due to cerebrospinal fluid collected outside of the membranes. This swelling became very marked and the patient complained of a great deal of headache. Consequently he was ordered to bed with high shock blocks under the foot thereof. On October 8th I aspirated from this swelling three ounces of clear cerebrospinal fluid, but the next morning the swelling was as large as ever. The condition remained about the same up to October 21st, when, as he had become very tired of hospital life, I let him return to his home in the country.

On December 29, 1903, I received a letter from him in which he says among other things: "In regard to the improvement of my case, will say that the gathering (*sic*) in my back has disappeared altogether. It disappeared within a very short while after my return home and has never returned. My headaches have also disappeared. I had several in the first week of my return, but with the disappearing of the fluid in the back my headaches went also. I am slowly but surely gaining. I go all around without a cane, but the walk is very awkward, something like one under the influence of liquor, yet I can see great improvement in that also. If I were in the dark I would not take a step or I would fall down, but now I can get around a great deal better in the dark.

"One feature of the case is very peculiar; it is the changes in my legs. The one that used to be my stronger before the operation is now my weaker one. The one I used to walk on altogether at first would break in the knee and I would fall down and the leg (the left one) feels very strong. I had to depend on it almost altogether

for a while after the operation. There is also a peculiar tightness in the left knee.

"I do all the chores here—five horses and six cows to attend. I also chop down trees, saw them up alone, and split it up into cord wood. I put up almost a cord in a day. Work does not bother my back at all, but does bother my kidneys some."

Since writing the above the patient has returned to the city and is now walking freely and without discomfiture. He is the janitor of a club-house, and is daily doing hard labor.

On March 26, 1904, I made an examination of him at my office, with the following result: The wound is firmly healed and the motions of the spine are freely and easily executed. The patient says that he has no complaints of any kind, that he feels as well as he ever did excepting for a severe cold which he now has. There is no Romberg symptom. The left great toe has a tendency to catch on the floor in the bare-foot gait, but still the walking is about perfect. The patient can place the weight of the body on either limb and swing the other leg backward and forward freely and easily. The knee-jerks are exaggerated on both sides, but the muscular power in both legs is normal. There is a slight tendency to patellar clonus on both sides and a moderate degree of ankle clonus on both sides, but it soon ceases. The cremasteric reflex is present on the right side, but absent on the left side. Both plantar reflexes are present and there is no Babinski on either side. Sensation to touch and pain in the left leg is normal, but on the external surface of the right leg to a point midway between the external malleolus and the head of the fibula sensation to pain is somewhat blunted. There is no inco-ordination in either leg; the patient can touch either patellar with the heel of the opposite foot quickly and accurately. The umbilical reflex on the left side is absent, but is present on the right side. The temperature sense is slightly confused on the right side of the abdomen and along the outside of the right leg.

#### Leg measurements:

Right leg	5 inches below the lower margin of patella	. . . .	13 inches.
"	" at lower margin of patella	. . . .	13¼ "
"	" 10 inches above the lower margin of patella	. . . .	19 "
Left	" 5 inches below " " "	. . . .	12¾ "
"	" at lower margin of patella	. . . .	13 "
"	" 10 inches above the lower margin of patella	. . . .	19 "

REMARKS. In the first place, it is to be noticed that when the patient was shot he fell in his tracks and remained completely paralyzed in his legs, and also as regards his bowels and bladder, for two weeks. This should make us cautious in accepting the dictum that when this state of affairs occurs we can never expect anything like a complete recovery.

Secondly, in the performance of the operation I cannot speak too highly of the method of boldly and quickly cutting down on one side of the spines, disregarding the free hemorrhage which is sure to occur, and then, having packed the wound with gauze wrung out in very warm water, going to the other side of the spines and doing the same thing; in this way alternating from side to side until the spines and arches have been completely cleaned down to the transverse processes. This procedure reduces the loss of blood to a minimum.

Thirdly, it is to be noted that whereas the external parts of the wound healed beautifully, it is quite evident that the membranes over the cord did not unite for a considerable time thereafter. I was advised, by what I consider to be the very best of surgical authority, to reopen the wound and resuture the membranes, but subsequent events proved that it was best to have waited.

In the fourth place, I was fortunate in having a competent neurologist associated with me. Nevertheless the present neurological localization brought the lesion somewhere between the fifth and twelfth dorsal vertebræ. Indeed, then, how much of credit must be given to the Roentgen method of exact localization to the horizontal plane of the body of the eighth dorsal vertebra. Had I been equipped with Dr. Sweet's admirable localizer I undoubtedly could have located the exact position of the bullet.

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## GONORRHOÆAL URETHRITIS, WITH UNUSUAL COMPLICATIONS.<sup>1</sup>

BY DANIEL CROSBY, M.D.,  
VISITING PHYSICIAN TO ALAMEDA COUNTY HOSPITAL.

**PATIENT**, a Mexican laborer, aged thirty-one years, unmarried. Admitted to Alameda County Hospital June 12, 1903; brought in by constable.

*History.* Little history obtainable, first, because of the somewhat delirious condition of the patient; second, because of the inability of the patient to understand English. Gonorrhœa contracted about three weeks ago. Inflammation of the eyes began about five days ago, and during these five days he lay unattended in an outhouse.

*Examination of Patient.* Half delirious, well-developed and well-nourished man of apparently thirty-five years. Eyelids greatly

<sup>1</sup> Read before the Alameda County Medical Association.

puffed, reddened, and discharging a stream of greenish-yellow pus. Conjunctivæ swollen so much as to become folded out between the lids and having the appearance of cotton placed between the lids to keep them separated. Within the lids conjunctivæ much injected and chemosis marked. Each cornea bordered by swollen conjunctiva formed a basin, as it were, which was full of pus, and the first conclusion was that the cornea was very much ulcerated. Upon cleansing the eyes each cornea was found only slightly ulcerated, but both were found very hazy.

*Nose and lips* very much swollen and congested. Thick, greenish-yellow pus discharging from nose and mouth. When this was washed away small ulcerations were to be seen not only within the nose, but also within the buccal cavity, upon the tongue, and upon the vermilion border of the lips. Salivation present. Jaws opened with great difficulty and pain. Gums spongy and retracted from all the teeth. Greenish-yellow pus exuding from every socket. Palate, pillars of fauces, and tonsils also ulcerated.

*Chest* shows dulness, with increased fremitus in the upper portions of both lungs anteriorly and posteriorly. Breath sounds were tubal in character. In both axillary regions dulness, decreased fremitus, and area of dulness changing boundary lines corresponding to changes in position by patient.

*Respirations* 42, labored and apparently painful.

*Heart.* No abnormality of size or position; sounds clear, accentuated. Pulse 120, full, strong.

*Abdomen.* Nothing abnormal.

*Penis.* Usual signs of acute urethritis.

*Microscopic Examination.* All secretions examined and all found to abound in gonococci.

*Diagnosis.* Acute gonorrhœa, gonorrhœal ophthalmia, and gonorrhœal infection of the nasal and buccal mucous membranes. Lobar pneumonia and pleurisy, with effusion.

In the forty-eight hours which elapsed from the entry of the patient until his dissolution the œdema and inflammation of the lids subsided somewhat, and it became easier to open them for the purpose of irrigation, even though the restless delirium of the patient prevented a very efficient course of nursing.

*Autopsy.* Strong, muscular individual; well nourished. Face swollen and discolored. Region of parotids and the entire scalp cedematous. Eyes, nostrils, and mouth full of pus. Eyes flattened and apparently collapsed. Nose greatly swollen and ulcerated without and within. Lips puffed up. Vermilion borders ulcerated and covered with greenish-yellow pus. Teeth can be lifted from sockets and roots are bathed with pus.

Abdomen distended; end of penis half covered with drying pus.

Intestines, stomach, and liver normal; spleen enlarged about one-third and softened; both kidneys congested and both pelves are filled with greenish-yellow pus. Ureters and bladder contain pus of same character.

The chest surface of pleuræ is coated with thick, greenish-yellow pus; left pleural cavity contains about 1000 c.c. of thin, purulent fluid; right contains about 400 c.c. of similar fluid. Large, suppurating areas occupy the greater part of the left lung and about one-half of the right; trachea and bronchi are filled with thick, creamy, greenish pus, of entirely the same character as that which has been discharging at the nose and mouth.

Pericardium contains about 75 c.c. of serum slightly tinged with blood. Heart muscle softened, but although the endocardium has lost its transparent sheen there are no indications of any ulcerations. No vegetations.

Cranial membranes under frontal lobes injected; optic thalamus markedly so. Remainder of contents of cranium not abnormal. Orbital fossa opened from behind and marked inflammatory condition noted. Ethmoidal cells are filled with pus having all the characteristics of all of the pus previously noted.

Smears from and sections of all tissues examined removed for microscopic examination. No culture made because of absence of proper culture media.

*Microscopic Examination.* Smears from penis, eyes, nose, mouth, ethmoidal cells, trachea, pleuræ, pelves of kidneys, and bladder without exception show diplococci which respond to Gram's decolorizing test and which have all of the characteristics, apparently, of the diplococcus of Neisser. However, some staphylococci were also present. In the secretion from the mouth a straight bacillus somewhat larger than the bacillus of tuberculosis, but not responding to the tubercle bacillus stain, was found. Aside from the straight bacilli mentioned and the staphylococci practically no bacteria were seen but the gonococci.

Sections of the suppurating areas in the lungs show that the condition of the lung is not so much a pneumonic condition as the formation of abscesses with the staphylococcus as the exciting agent.

Sections were made by Professor Ophuls, of Cooper Medical College.

I am aware of the very material defect in this report in that a culture was not made of the pus. Unfortunately, its reaction to stain does not absolutely identify this mischievous little organism. We need to see it grow. However, its staining characteristics together with the history of the case warrants us, I think, in assuming that our conclusions are correct.

In looking over the literature on the subject I do not find very

much bearing upon it. After the identification of the gonococcus by Neisser in 1879, Bumm showed that decolorizing by Gram's method is an essential procedure for the proper recognition of the diplococcus. We see references to cases of extensive infections in which the gonococcus is accompanied by many pus cocci, and one case is reported in which a patient suffered from gonorrhœa with double orchitis and general septic infection with endocarditis, in which the gonorrhœa had no part in the sepsis, but which was caused by a large dumbbell-shaped coccus which stained beautifully by Gram's method.<sup>1</sup>

Cardile<sup>2</sup> reports a pleurisy developing one month after infection with gonorrhœa. Pus, both morphologically and upon cultivation, showed characteristics of the gonococcus. Complete recovery.

West<sup>3</sup> refers to a *résumé* of the subject by Faitout and upon the demonstration of the gonococcus both by microscope and by culture.

Bertrand<sup>4</sup> says that pleurisy following gonorrhœa may be dry or effusive, usually mild and short.

Anders<sup>5</sup> refers to gonorrhœal arthritis with pleurisy and embolic septic pneumonia.

Lartigau<sup>6</sup> reports a case of gonorrhœal endocarditis in which the specific organism was demonstrated in the heart blood and in the vegetations on the valves. He refers to Thayer and Lazear, who obtained a pure culture from blood and from heart and pericardium post-mortem. Also to Rendu and Halle, who obtained a pure culture from the endometrium, from the exudate in the elbow joint, and a pure culture from the heart lesion.

Dauber and Borst<sup>7</sup> report malignant endocarditis of aortic valves a few weeks after the acquisition of gonorrhœa. Microscopic examination of valves, blood, abscess on aortic valve, and splenic pulp revealed abundant presence of a diplococcus which, morphologically, had all of the characteristics of a gonococcus. All nutrient media save a serum-agar tube remained sterile, but the growth upon this was not considered to be gonococci.

Lenhartz<sup>8</sup> obtained a pure culture from the aortic valve and with it inoculated successively a healthy human urethra.

Thompson<sup>9</sup> quotes Hernig as having demonstrated the diplococcus upon the heart valves, and Councilman as having found them in the cardiac muscle.

Jicinsky<sup>10</sup> reports a case of pleurisy following gonorrhœa, but his conclusions are not substantiated by cultures.

Jessionek<sup>11</sup> reports a case of stomatitis preceded by double gonorrhœal conjunctivitis. He describes round, grayish-white patches on the surface of the tongue and cheeks. Much swelling and soreness and evidence of inflammation of sublingual glands. Cover-glass preparations and cultures showed gonococcus.

Sidney Vines<sup>12</sup> reports a case of gonorrhœal gingivitis following



gonorrhœal urethritis: "Infection of urethra March 22d. April 16th, complained of sore mouth and having to spit often. Gums red, swollen, spongy; an overabundant supply of saliva. Condition resembled a mercurial stomatitis. By April 20th he presented an appalling spectacle. Huge, incapable, with big head, of bulldog sort, the lower jaw drooping, saliva unceasingly trickling from the angles of his mouth, and every tooth loose and bathed in pus which oozed from every socket. He could not eat, and drank with difficulty. Temperature, 101°. Atmosphere of the bedside very offensive. April 22d, gonococci demonstrated in the pus. May 10th, mouth normal." This patient had been in the habit of picking his teeth, every day after eating, with a splinter of wood which he had whittled down.

Holder<sup>13</sup> reports the case of a man who had buccal coitus with a man suffering with gonorrhœa. On the next day he complained of pain in the lips and gums. On the fourth day mucous membrane of lips and buccal cavity intensely red; gums spongy, with a tendency to bleeding and receding from the teeth, and the buccal secretion became much increased in quantity. Motion of the mouth was very painful. Holder states that the affection begins with a sensation of heat and dryness of the mouth, which at first appears very red. Soon a purulent discharge flows from the swollen and inflamed parts, which may be covered with an aphthous-like exudation.

Cutler<sup>14</sup> reports a case of gonorrhœa of the mouth following coitus ab ore. On morning following, mouth raw and sore and with "horrible" taste. On second day little sores appeared on lips, and on third day the gums and tongue were swollen and painful. By the fifth day the whole buccal cavity was so inflamed that she could not eat and a whitish fluid mixed with blood and having a very unpleasant odor was secreted.

*Examination.* Mucous membrane of lips and cheeks red, denuded of epithelium in spots and covered with specks of false membrane which were readily detached, leaving an excoriated surface. Gums swollen, retracted from teeth, and bled very readily on pressure. Tongue swollen and very tender. It could be only slightly protruded and then only with much effort and pain. Its surface was red and glazed and covered with small ulcers which secreted a thick, yellow pus. The soft palate and pillars of the fauces were very much inflamed, but parts beyond were in normal condition. Breath was very offensive. Little salivation. The mouth secretion was seen to consist of pus and epithelial cells and a large quantity of bacteria. In the false membrane an organism resembling the gonococcus was found, but its identity was not established absolutely.

So much for the recital of reports of infection by the gonococcus,

It is of some interest to note the extension of the disease in the patient under consideration.

The urethral infection was undoubtedly the primary one and that of the eyes next. It is logical to suppose that the infection went thence to the nose and mouth. The infection of the lung was apparently not gonorrhœic in character, although the pus in the pleura had entirely the microscopic appearance of gonorrhœal pus. This may also be said of pus that was removed from the trachea above its bifurcation.

There was no evidence of endocarditis; so the trouble in the lung can perhaps be referred less to the blood stream than to inspiration.

With reference to the portals of infection of the pleura Grober records some experiments that are of some interest. He found that forcible inhalation of finely powdered stains resulted in the appearance of granules in the parietal and visceral pleura and the discoloration of the lymph channels along the borders of the ribs. The same experimenter injected stains into tonsils and found stain in lymph channels and glands down the neck and in lymph channels of the lower mediastinum.

This may, perhaps, give us a clue to the origin of the gonococcus infection of the pleura; but whether from this path or the blood stream we are forced only to conjecture.

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## REVIEWS.

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A COMPEND OF THE PRACTICE OF MEDICINE. By DANIEL E. HUGHES, M.D., Late Chief Resident Physician, Philadelphia Hospital; Late Physician-in-Chief, Insane Department, Philadelphia Hospital; Formerly Demonstrator of Clinical Medicine in the Jefferson Medical College of Philadelphia, etc. Seventh Revised Edition, Edited, Revised and in Parts Rewritten by SAMUEL HORTON BROWN, M.D., Assistant Dermatologist, Philadelphia Hospital; Assistant Dermatologist, University Hospital Dispensary, etc. Including a Section on Mental Diseases and a very Complete Section on Skin Diseases. Illustrated. Philadelphia: P. Blakiston's Son & Co., 1904.

THIS posthumous edition of Dr. Hughes' book has been considerably rewritten and rearranged, as stated by the editor in his preface. It has thus been modernized and contains the latest theories and views on each subject. It needs but a brief mention of Dr. Hughes' exceptional opportunities for the study of disease in all its manifestations to show how peculiarly fitted he was to produce a work on general medicine. Dr. Hughes was for many years Chief Resident Physician at the Philadelphia Hospital, at which place he saw and had under constant observation not only numerous cases of the acute diseases, but an unusually varied and large assortment of chronic diseases, particularly nervous diseases. He also had opportunities to study a great number of cases of mental diseases of all varieties and in all stages. He was also able to widen his views through contact with the attending physicians, who in many cases had other sources for gaining experience.

So many topics are considered in this compend that a bulky volume necessarily results, but the use of thin paper and flexible covers make it surprisingly compact and easy to read. The consideration of each subject is divided into paragraphs devoted to the etiology, pathology, prognosis, differential diagnosis, and treatment; and while unessential matters are only briefly mentioned, and in no case is there a long description of any one feature, an excellent account of each disease is given. The characters that make the book of most use from a practical point of view are the numerous prescriptions and suggestions for treatment and the

paragraphs on differential diagnosis which mention and contrast the various conditions which may be confounded. The subjects are grouped under the proper divisions and a brief general discussion precedes each section, while in the case of gastrointestinal and renal diseases and blood diseases the diagnostic technique is described so that methods of clinical diagnosis in common use are to be found.

The volume is so arranged and its contents are of such a high character that it should be of service to the physician whose time is so occupied that he cannot consult the larger text-books, or to one who wishes merely to refresh his knowledge and to fix in his mind the essential facts freed from details.

F. W. S.

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BURDETT'S HOSPITALS AND CHARITIES, 1905: BEING THE YEAR BOOK OF PHILANTHROPY AND THE HOSPITAL ANNUAL. By SIR HENRY BURDETT, K.C.B. London: The Scientific Press, (Ltd.).

THIS invaluable work has established itself so firmly as an absolute necessity for those who are interested in hospitals and charitable enterprises that it hardly needs an extended review. It not only presents a street directory, but it gives the executive staffs, the number of patients, income and expenditure of practically every hospital and institution dealt with. Each year has seen some improvement in the general arrangement of the work, rendering it more useful, and the vast amount of information within it more accessible. It covers practically every charitable institution in Great Britain, the British Colonies, and the United States, including not only hospitals and institutions concerned in the care of the sick, but also orphanages, homes, and aid and rescue societies. The information contained within it is so carefully compiled from authoritative sources that it may be absolutely relied on. J. H. G.

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RADIOTHERAPY AND PHOTOTHERAPY. By CHARLES WARRENNE ALLEN, M.D. Illustrated with 131 engravings and 27 plates in colors and monochrome. New York and Philadelphia: Lea Brothers & Co., 1904.

DR. ALLEN has devoted the major part of his work to radiotherapy, in which his experience with the Roentgen rays is most extensive. He gives sufficient explanation of the principles and apparatus to render the subject clear to his readers without too much elabora-

tion of detail, which is often more confusing than helpful. His chapter on methods of administration and protection are valuable to every operator, while his warning against the dangers to the operator himself are timely, though possibly not sufficiently strong. This subject is one which should receive special emphasis from every author who desires to further the best interests of those he would instruct. Medical and surgical diagnosis receive a concise review as is fitting in a work primarily devoted to therapy.

In the description of technique, the author appreciates keenly the necessity of developing a more accurate method of dosage, and strives to indicate methods by which it can be attained. Progress is the characteristic of this method of therapy at the present time, and so rapid is this progress that it demands almost quarterly editions to keep pace with the advances in technique. More accurate instruments for measuring dose are already at hand, and their character and use will doubtless appear in the next edition, as also the variations in technique, which adapt this therapeutic agent to the various manifestations of malignant disease in superficial and deep situations. The reason why therapeutic action takes place on the opposite side of the surface treated, as the ear or nose, will then be explained.

The chapters on Light, Actinotherapy, Radioactivity, and High-frequency Currents are timely, but serve to show that those therapeutic agents are inferior to the Roentgen rays, both because they are much slower in action and because their potency is vastly inferior.

The work, on the whole, leaves little to be desired, though it is fair to say that at the present time the best views and latest technique can hardly be expected outside of current literature. It is impossible to teach experience in a book, but the author's aim should be to give his readers all the knowledge he can gather that will further their search for experience.

C. L. L.

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MANUAL OF PHYSIOLOGICAL AND CLINICAL CHEMISTRY. By ELIAS H. BARTLEY, B.S., M.D., Ph.G., Professor of Chemistry, Toxicology and Pediatrics in the Long Island College Hospital; author of *Medical and Pharmaceutical Chemistry*. Second edition, revised and enlarged, with 47 illustrations. Philadelphia: P. Blakiston's Son & Co., 1904.

THIS book of 188 pages contains a great many things and many more subjects are treated than one would judge from its title. A large part of the book is taken up by a description of methods used in clinical chemistry and clinical diagnosis. Many of the methods

are given incompletely, or in such a way as to be valueless as a laboratory guide. At times comments are made upon the clinical significance of the various findings by the methods, but these additions seem to be at random. A number of laboratory experiments to bring out the properties of various organic substances are found from time to time as one reads the book. Clinical examination of the blood is treated in five and one-half pages, and although the author apologizes for the section in the preface it is obvious that he would have done better to have omitted it. Other subjects of slight importance or of questionable clinical application are treated at some length. For instance, several pages are devoted to cryoscopy of the urine. Milk modification is also discussed.

The book is without a table of contents, and its arrangement is poor. It is difficult to see to what class of readers the book would prove of use.

G. C. R.

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THE TREATMENT OF FRACTURES: WITH NOTES UPON A FEW COMMON DISLOCATIONS. By CHARLES LOCKE SCUDDER, M.D., Surgeon to the Massachusetts General Hospital. Fourth edition, thoroughly revised, with 688 illustrations. Philadelphia, New York, and London: W. B. Saunders & Co.

THE fact that this book has passed through four editions since it first appeared in 1900 is sufficient proof of its worth. In addition to some alterations in the text, there has been considerable change and improvement made in the illustrations. An entirely new chapter, but a brief one, on the subject of Some of the Common Dislocations, has been added. This book certainly presents the subject of the treatment of fractures in a most thorough and complete manner. It is to be especially commended upon the clearness of the text and the excellence of the illustrations, which enable the reader to understand and practice the various manipulations and dressings described.

We feel that we must repeat a criticism made of one of the earlier editions, and that is that we think the time suggested for active and passive movements of the fingers and wrist in fracture about the lower end of the radius is not early enough. We believe that the movement of the fingers in these fractures should be commenced practically at the first dressing, since, if properly done, there is not the slightest danger of displacement of the fragment, and the restoration of function is much more prompt. Another criticism that is of minor importance, but which might be mentioned, is that the author speaks of the angular splint applied to the front of the upper extremity as an "internal" angular instead of "anterior" angular.

Taking it as a whole, this is one of the best works on the treatment of fractures with which we are acquainted.

J. H. G.

GALLSTONES AND THEIR SURGICAL TREATMENT. By B. G. A. MOYNIHAN, M.S. (London), F.R.C.S. Philadelphia, New York, and London: W. B. Saunders & Co., 1905.

THE author of this volume need make no apology for devoting so much space to the single subject of gallstones, and the reader will certainly not think of asking for one. The subject is most important both from the point of view of the surgeon and that of the internist, and therefore a practical dissertation such as this is of the greatest value. The author has had an unusually large experience in the surgery of the gall-bladder and its associated organs, and is consequently thoroughly fit for the task. The book should be read by medical men in order that they may see the results of neglected gallstone disease and compare the operative treatment of such cases with that of the uncomplicated ones, and also in order that they may understand the symptoms to which the surgeon attaches most value in the catastrophies which occasionally take place in diseases of the gall-bladder.

The surgeon can learn much from a careful study of Moynihan's technique, which is described very fully and comprehensively. After discussing the anatomy of the gall-bladder and ducts and the varieties of gallstones, considerable space is devoted to the pathology and especially to the symptoms of gallstone disease.

The portion of the book dealing with this subject is beautifully illustrated, which greatly enhances the value of the work.

All of the various operations upon the gall-bladder are described in detail. The reader will observe that the author, like so many surgeons of extensive experience in this line of work, has greatly extended the indications for the operation of cholecystectomy.

The work we can heartily recommend as most satisfactory and of the greatest practical value, especially to the surgeon.

J. H. G.

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A TREATISE ON DISEASES OF THE NERVOUS SYSTEM. By L. HARRISON METTLER, A.M., M.D. Chicago: Cleveland Press, 1905.

DR. METTLER believes that "the neurone doctrine is now an accepted fact," and that "its teachings have done more to illuminate the dark places of neurology than has any single scientific generalization heretofore promulgated." He bases his work on these two statements and hopes that the student will be able "to behold the entire field of neurology under the brilliant illumination cast upon it by this scientific generalization." It is a dangerous thing to base a medical book upon a theory, because theories have a habit of going out of fashion and the neurone doctrine is not as

fashionable as it was a few years ago. Apart altogether from theory the descriptions of disease are for the most part clear and the therapeutic directions excellent. We hope that when a new edition is issued lighter paper will be used, because it is cruel to expect anyone to hold and study a book weighing six and a half pounds.

C. W. B.

**ELECTRICITY IN EVERY-DAY LIFE.** By EDWIN J. HOUSTON, Ph.D.  
In three volumes; illustrated. New York: P. F. Collier & Son.

ALTHOUGH these three volumes are hardly to be considered as medical works, they nevertheless contain information which is of value to every physician who is desirous of availing himself of the most recent knowledge in the ever-progressing subject of electricity. The applications of electricity to medical science are increasing daily. It is impossible for a doctor to really study the subject, and a book such as this enables him to grasp the essentials necessary to a working knowledge and enables him to use the various electric appliances with which every well-to-do office is equipped with some understanding of the nature of the elements which he employs. Dr. Houston's explanations of the scientific problems involved and his descriptions of apparatuses and technique are so practical and clear that a layman can grasp them and apply them to his uses with the greatest ease. Aside from its technical value the book is charming reading, and its delightful accounts of the wonderful discoveries and inventions which have succeeded one another since Benjamin Franklin's famous kite-flying experiment will speak to all and stimulate a desire to know more of a wonderful subject.

F. R. P.

**THE DOCTOR'S RED LAMP. A BOOK OF SHORT STORIES CONCERNING THE DOCTOR'S DAILY LIFE.** Selected by CHARLES WELLS MOULTON. Chicago, Akron (Ohio), and New York: The Saalfield Publishing Co., 1904.

THIS book contains twenty-two short stories dealing with the life of the doctor. Curiously enough, the stories are almost all of them by laymen. As the editor says in his preface, many of them are old favorites, a fact which will probably appeal all the more to those who see the book. They have been well chosen, and their perusal will, we hope, give many a physician a number of pleasant hours of recreation. The idea of a series of books of this nature



is a good one and its execution is commendable. If the editors continue to show the discretion and good sense which is manifested in their choice of material, the books should commend themselves to every physician. The volume is accompanied by four handsome illustrations appropriate to the text. F. R. P.

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APPLETON'S MEDICAL DICTIONARY: AN ILLUSTRATED DICTIONARY OF MEDICINE AND ALLIED SUBJECTS IN WHICH ARE GIVEN THE DERIVATIONS; ACCENTUATION, AND DEFINITION OF TERMS USED THROUGHOUT THE ENTIRE FIELD OF MEDICAL SCIENCE. Edited by FRANK P. FOSTER, M.D., editor of *The New York Medical Journal* and *Philadelphia Medical Journal*, consolidated; of a *Reference Book of Practical Therapeutics*; and of *Foster's Illustrated Encyclopædic Medical Dictionary*. New York and London: D. Appleton & Co., 1904.

BECAUSE of the rapid advance which has been made in nearly all lines of medicine and surgery during recent years there has arisen a demand for newer and more complete medical dictionaries. It has been the aim of the publishers and editor of this volume to satisfy this demand, and that they have done it there can be little doubt.

The book contains an enormous amount of information, especially regarding anatomy and diseases. It has not adopted some of the newer methods of spelling which have become so prevalent, but for this we can only commend it. The definitions are very clear and satisfactory.

The one criticism we would make is that probably too much has been put under single headings and consequently the person who consults the book for a definition instead of finding the word in large type may have to look through possibly a page of subheadings; as for instance, Littré's hernia, which is indexed under hernia, but not under Littré. Richter's hernia we do not find mentioned at all. Neither Bright's disease nor Graves' disease can be found excepting under the general heading of Disease, there being no cross-reference to the same. We believe it to be wrong to attach proper names to diseases and operations, but nevertheless certain of these have become so firmly fixed in our nomenclature that they should at least be given a cross-reference.

Notwithstanding this criticism, which of course does not depict a serious defect in the work, we believe that this dictionary will be found a most satisfactory book of reference. The illustrations are not so frequent as in most modern dictionaries, but illustrations are not nearly so essential to a dictionary as to a modern text-book.

J. H. G.

MENTAL DEFECTIVES, THEIR HISTORY, TREATMENT, AND TRAINING. By MARTIN W. BARR, M.D. Philadelphia: P. Blakiston's Son & Co., 1905.

DR. BARR has lived with and studied "mental defectives" for about twenty years; a book therefore written by him ought to be of value, and this is one of the most practical and useful books for the care of the feeble-minded that has been written. The keynote of the book is the following: the hopelessness of cure and the needless waste of energy in attempting to teach an idiot, what may be attained in training the imbecile, and the urgent need of preventing the backward child from degenerating into imbecility, and finally the necessity of safe-guarding the immoral imbecile from crime. No attempt is made to explain the pathology and morbid anatomy of idiocy and imbecility.

Dr. Barr is strongly in favor of asexualization as a means of preventing the propagation of idiots and imbeciles. He believes these conditions are largely hereditary and that the State should appoint surgeons and neurologists to operate non-improvable cases in institutions. If such a function as this properly belongs to the State, then it ought also to asexualize paranoiacs, many cases of insanity, and not a few alcoholics and hysterics, for all of these propagate degenerates. Very few idiots propagate, and the imbeciles that are sexually strongest are those of the higher grade who are or seem to be improvable. The State Assembly has just passed a law doing what Dr. Barr desires. It is now awaiting the Governor's decision. We think the law pernicious because it extends the functions of the State too much and thus no good will come from it as the dangerous cases will not come under it.

A very large part of the book is filled with the histories of illustrative cases. Every one interested in mental defectives and their care, whether physicians, judges, teachers, or persons interested in the study of juvenile crime, should read and own this book.

C. W. B.

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ESSENTIALS OF NERVOUS DISEASES AND INSANITY, THEIR SYMPTOMS AND TREATMENT. By JOHN C. SHAW, M.D. Fourth edition, thoroughly revised by SMITH ELY JELLIFFE, M.D., Ph.D. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THIS is a very good little book for the purpose of which it was intended, namely, as a primer for advanced students. It concerns itself principally with diagnosis. All anatomical and physiological details are omitted. The first 150 pages are devoted to nervous diseases, the next 40 to mental diseases. It is written in clear English and the illustrations are very good.

C. W. B.

ATLAS AND EPITOME OF GENERAL PATHOLOGICAL HISTOLOGY. By DOCENT DR. HERMANN DURCK, of the Pathological Institute, Munich. Authorized translation from the German. Edited by LUDWIG HEKTOEN, M.D., Professor of Pathology in Rush Medical College, Chicago. With 176 colored illustrations and 80 lithographic plates and 36 figures in black and colors. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

To anyone who has been familiar with the exquisite colored plates in the original edition of Dürk's *Atlas and Epitome of General Pathological Histology*, the present English edition, edited by Dr. Hektoen, will be exceedingly gratifying. The beautiful illustrations, reproduced with the greatest care and accuracy, are almost sufficient in themselves to teach the subject. The accompanying text is, however, only explanatory, and reviews the vast field of general pathology in a brief and lucid manner. The original suffers few changes in the translation. Occasionally the editor has inserted short notes, which always add to the value of the paragraph.

The student of pathology, who does not read German, is fortunate to have this book made available for his use. W. T. L.

THE MEDICAL EPITOME SERIES. SURGERY. A Manual for Students and Practitioners. By M. D'ARCY MAGEE, A.M., M.D., Demonstrator of Surgery and Lecturer on Minor Surgery in the Georgetown University Medical School, and WALLACE JOHNSON, PH.D., M.D., Demonstrator of Pathology and Bacteriology, Georgetown University Medical School. With an Appendix on *x-ray* Work in Surgery by EDWARD O. PARKER, A.M., M.D., Physician at the New York Dispensary. Series edited by V. C. PEDERSEN, A.M., M.D. Illustrated with 129 engravings. Philadelphia and New York: Lea Brothers & Co.

ONE can easily realize the difficulty of epitomizing general surgery in so small a book as the present volume, and possibly anyone undertaking such a work will be criticised by his reviewers for devoting too little space to some subjects and too much to others. The present book is open to this criticism, as can be seen by a reference to the chapter on Fractures and to that on the *x-rays*.

In most respects, however, the book is very satisfactory. The illustrations are especially good. We believe that the list of questions at the end of each chapter is a good idea, as it causes the student to review the text and also to formulate some idea of the subjects which he has studied. The views expressed by the author are in accord with the most advanced surgical authorities, and are expressed in a way well adapted to the need of the student. J. H. G.

ESSENTIALS OF MATERIA MEDICA, THERAPEUTICS, AND PRESCRIPTION WRITING. By HENRY MORRIS, M.D., Fellow of the College of Physicians of Philadelphia, etc. Sixth edition, thoroughly revised by W. A. BASTEDO, PH.G., M.D., Tutor in Materia Medica and Pharmacology at Columbia University (College of Physicians and Surgeons), New York, etc. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THIS little book bears evidence of careful revising and should be useful for a review of the subjects treated therein. We imagine, also, that examiners may find it convenient in framing papers. While it can never supplant the systematic text-book, for it lacks breadth and perspective, the care in compilation and conciseness of expression have made for it a field of usefulness of which its popularity is good evidence.

R. W. W.

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MULTIPLE PERSONALITY, AN EXPERIMENTAL INVESTIGATION INTO THE NATURE OF HUMAN INDIVIDUALITY. By BORIS SIDIS, M.A., Ph.D. (Harvard), and SIMON P. GOODHART, Ph.B. (Yale), M.D. New York: D. Appleton & Co., 1905.

THIS book is interesting but unsatisfying. One takes it up hoping to have solved one of the greatest problems of psychology and having read it is no wiser than before. One hundred and fifty-three pages are taken up with the history of one case. This is interesting reading, but one feels he is at the mercy of the intellectual accuracy of the patient, and people who pass through such experiences as he did are not always accurate in their statements. There is growing up a school of mystical materialism, if one may couple two words so apparently contradictory, and this book seems to belong to that school. It is very interesting, but "the nature of human individuality" is not explained by it.

C. W. B.

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BEAUTY THROUGH HYGIENE. By EMMA E. WALKER, M.D. New York: A. S. Barnes & Co., 1904.

THIS volume, one of the *Woman's Home Library* series, is a collection of clearly written articles on "Common-sense Ways to Health for Girls," as the title-page announces. To readers of a prominent magazine for women portions of the book will seem familiar, but certain truths bear repeating, and in this case Truth and Beauty are indeed one. While probably few women would have the time, and fewer still the patience to carry out all the doubt-

less valuable suggestions contained in these pages, yet most of the advice is worth taking, and ought to appeal not only to the woman reader, but also to those who have the guidance of young girls who are at the age when the formation of daily habits of personal hygiene is most important.

J. P. G.

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DISEASES OF THE LIVER, GALL-BLADDER, AND BILE-DUCTS. By H. D. ROLLESTON, M.A., M.D. (Cantab.), F.R.C.P., Physician to St. George's Hospital, London; Formerly Examiner in Medicine in the University of Durham; and Fellow of St. John's College, Cambridge, England. Fully illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1905.

THERE have been many good books written on the liver—Glisson in the seventeenth, Bianchi in the eighteenth, Frerichs, Budd, and Murchison in the nineteenth centuries. Of modern works, that of Frerichs, issued in 1858 and reproduced in the New Sydenham Society's publications, has remained without rival in any language, and now this treatise of Rolleston's easily takes a place beside it. There has not been for years issued from the press so comprehensive and accurate a consideration of the diseases of an important organ. In every way it will rank as a masterpiece, and reflects the highest credit upon British medicine. Dr. Rolleston has been a well-known student of diseases of the liver, but very often the special concentration on a subject unfits a man for a wide view of its problems. But this is in every way a model work, showing an unusually large personal experience with a range of reading quite unusual, even in these days of accurate bibliography. It would be difficult to mention a recent work which represents so truly the cosmopolitan character of medicine. Tribute has been collected from every country, and had Dr. Rolleston been a Frenchman, a German, or an American he could not have shown greater familiarity with the native literatures. American contributions to the subject are most fully and satisfactorily represented. It is remarkable how familiar the author is with the writings of physicians on this side of the water.

It is difficult to select a special section for commendation where all are so good, but the concluding chapter on cholelithiasis, extending over some seventy pages, may be referred to as a model of its kind. The subject is treated with great fulness, and equal consideration given to the medical and chirurgical sides of the many problems which are at present before the profession.

The writer's style is admirable, clear, and to the point, and his judgment on questions is enforced by an evident desire for fairness. The work should appeal to a large class of readers. It will take its place on the book-shelves of every careful practitioner who wishes

a helpful guide in this important class of diseases. To the surgeon and specialist it will prove invaluable, while to the student of the many problems in hepatic pathology still awaiting solution it will prove an authentic guide of the highest order. E. Y. D.

THE SURGERY OF THE DISEASES OF THE APPENDIX VERMIFORMIS AND THEIR COMPLICATIONS. By WILLIAM HENRY BATTLE, F.R.C.S., Surgeon to St. Thomas' Hospital, etc., and ELDRED M. CORNER, M.B., B.C., F.R.C.S., Surgeon in Charge of Out Patients to St. Thomas' Hospital, etc. Chicago: W. T. Keener Co., 1905.

THIS small volume, comprising about 200 pages, contains some very useful information on the subject of appendicitis, which it states in a very clear and concise manner. A brief, interesting history of the disease is given, and considerable space is allotted to the discussion of the diagnosis and the various complications of the disease. The methods for the removal of the appendix are described, especially the one practised by the authors—*i. e.*, "temporary displacement of the rectus abdominis." The last chapter is devoted to the subject of the relation of appendicitis to the selection for life insurance, and a number of rules for insurance examiners are given. The book is well written and we can highly commend it to surgeons as well as general practitioners. C. F. M.

ELECTRICITE MEDICALE. Par le DOCTEUR H. GUILLEMINOT. Avec 79 figures dans le texte et 8 planches hors texte. Paris: G. Steinheil, 1905.

IN this book of 613 pages the author has given on the whole an excellent and conservative description of modern electrotherapeutics. In addition to those subjects, including the  $x$ -rays, usually treated of in such works, we find considerable attention given to the effects and employment therapeutically of agents having electricity as a generator—*i. e.*, ozone, vibratory massage, phototherapy, and thermotherapy. The newer forms of the electric current employed in medicine, as the sinusoidal, undulatory, and high-frequency, receive considerable attention. The sections upon the physics, physiological action, and therapeutics of currents of high frequency are of especial value, as would be expected from a French author, the electrotherapeutists of that nation having done so much for the advancement of this modality as a therapeutic agent. Under the description of the reaction of degeneration considerable space is devoted to possible explanations of the reasons for

the occurrence of this phenomenon and the experiments of Wiener, May, and Joteyko are fully detailed. A novel feature of the book is that instead of devoting a separate section to electrodiagnosis this is discussed in all cases in which the electricity is of aid in the diagnosis in connection with the description of the therapeutic procedures of use in the disease. This is an innovation in arrangement of considerable convenience. In this connection it is peculiar that two such valuable diagnostic aids as the myotonic and myasthenic reactions are not described. In discussing the treatment of aneurysm by electrolysis the excellent work of American operators, as D. D. Stewart, Hunner, and others, is not mentioned. The illustrations are not numerous, but among them are some very useful plates showing the motor points. These differ from those usually found in the text-books in that the motor points of all the muscles supplied by a certain nerve are represented by the same color; thus the motor points of all those muscles supplied by the median nerve are colored red, by the ulnar blue, and so on. This arrangement has also been independently adopted by Mosher, of Albany, in his work on electrodiagnosis. In conclusion it can be said that this book will prove of service to all interested in electrotherapeutics.

C. S. P.

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PNEUMONIA AND PNEUMOCOCCUS INFECTIONS. By ROBERT B. PREBLE, A.B., M.D., Professor of Medicine, Northwestern University. Illustrated. Chicago: Cloyd J. Head & Co., 1905.

DR. PREBLE'S subject is handled in the most satisfactory manner, the book considering pneumonia carefully in every aspect. A series of 3600 cases of pneumonia reported by six observers has been collected by the author, and these cases have been used in the compilation of statistical tables and charts bearing on almost every feature of the disease. By taking such a large number of cases reported by so small a number of men a high degree of uniformity of observation is secured; and since pneumonia differs to such a marked extent in different localities and in different years the average percentages are made nearly exact by the fact that the individual reporters are of different nationalities and report cases occurring in different epidemics. It is of distinct advantage to have definite figures showing the average frequency of occurrence of the various symptoms and complications and the average time at which these are likely to appear, and such figures are not readily found.

Outside of the statistical features there is little new or original matter in the book, but so much space is devoted to each symptom

and complication, with complete and practical descriptions of the diagnostic signs and technique in each instance, that the reader may obtain valuable information on this disease, which is undoubtedly becoming more prevalent.

A section is given to the study of the pneumococcus infections which may occur either independently or coincident with lesions in the lungs. In this connection it is urged that the blood culture and lumbar puncture be used in all doubtful cases in addition to the ordinary methods of diagnosis. Cases are cited in which pneumococcus meningitis and arthritis occurred without any pulmonary manifestations of the infection, and were mistakenly diagnosed as epidemic meningitis and rheumatism respectively, until blood cultures had been made.

In the section on treatment the various theories or modes of treating pneumonia which have been highly praised are discussed, and a statement of the practical results obtained at the hands of others than the discoverers is given. The author states as his opinion that no plan of treatment which has been advocated has so far proven to be specific in the test of frequent trials in varying places. He recommends symptomatic treatment as the method most likely to assist and least likely to injure the patient, and says that no treatment can be considered specific or thoroughly satisfactory until a reliable pneumococcus antitoxin has been perfected.

F. W. S.

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ESSENTIALS OF BACTERIOLOGY, BEING A CONCISE AND SYSTEMATIC INTRODUCTION TO THE STUDY OF MICRO-ORGANISMS. By M. V. BALL, M.D. Fifth edition, thoroughly revised by KARL M. VOGEL, M.D., Assistant in Pathology, College of Physicians and Surgeons, Columbia University, New York City. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

THE author and editor have succeeded in bringing together in a systematic manner the essentials needed in the study of bacteria. The style employed is concise, much of the book being written in the form of more or less expanded definitions.

Part I. consists of general considerations and technique, the latter subject being quite fully and well treated, forming the best part of the book. In considering the various bacteria, perhaps undue space is given to the non-pathogenic varieties, of which about thirty are discussed. A special chapter is devoted to the bacteria pathogenic for animals, but not for man, and the pathogenic protozoa are described. In an appendix various technical subjects, such as the examinations of air, water and soil, milk, and of the organs and cavities of the human body, are briefly discussed, and



a tabulation of both pathogenic and non-pathogenic organisms is given. The book is 243 pages in length and covers consisely the subject of bacteriology with a considerable degree of completeness, bringing it in most particulars up to date.

G. C. R.

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A MANUAL OF EXPERIMENTAL PHYSIOLOGY FOR STUDENTS OF MEDICINE. By WINFIELD S. HALL, Ph.D., M.D. (Leipzig); Professor of Physiology, Northwestern University Medical School, etc. Philadelphia and New York: Lea Brothers & Co.

THIS book is the published form of a manual which the author has used for some years in his teaching. It contains a series of experiments which quite thoroughly cover the field of physiology as taught to the medical students of to-day. The first chapter is on "Cytology," and the experiments in it are devised to bring out the fundamental activities of single-cell organisms, cilia, and the effects of various substances upon simple organic life. Electric apparatus is carefully explained in the following chapter dealing with the general physiology of muscle and nerve tissue. Chapters upon the circulation and respiration, normal hæmatology, digestion and absorption, vision, the nervous and muscular systems, complete the book.

The method generally employed is to explain first the appliances, then describe the methods of preparation and technique of the operations, and, lastly, the special points to be observed are given.

The book, which contains 245 pages, is especially valuable because, unlike the usual text-book upon physiology, it is stamped with the individuality of the teacher.

G. C. R.

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SURGERY OF THE PROSTATE, PANCREAS, DIAPHRAGM, SPLEEN, THYROID, AND HYDROCEPHALUS. AN HISTORICAL REVIEW. By BENJAMIN MERRILL RICKETTS, Ph.B., M.D. Cincinnati, 1904.

AN index to the surgery of the prostate, pancreas, thyroid, etc., would be a more comprehensive name for this book, as its pages are principally made up of references chronologically arranged from the literature pertaining to these different organs. A chapter is allotted to each organ; a brief description of its anatomy, etiology, and its pathological conditions are given, and the various surgical operations are described. The bibliography comprises the main part of the book and shows very careful and exhaustive work on the part of the author.

C. F. M.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**Heart Affections in Scarlet Fever.**—SCHMOLTZ (*Münchener med. Wochenschrift*, 1904, li. p. 1417) states while the cardiac lesions in diphtheria have been carefully studied, those occurring during and after scarlet fever have been more or less overlooked, owing probably to the infrequency of such serious and tragical results as follow diphtheria. In a study of 191 cases of scarlet fever, Schmoltz, of Dresden, found that about 35 per cent. showed signs of some circulatory disturbance. In the beginning of the attack the pulse is always rapid. This does not indicate any cardiac derangement. Indeed, later evidence of cardiac lesion is about as likely to appear in cases which at this period show a slow pulse as in those cases with marked acceleration. Of greater importance is the rate of the pulse at subsequent periods. When the temperature falls the pulse, as a rule, returns to the normal rate, but variations are observed. In some cases the rate becomes much diminished, while the temperature is still elevated. Pulses of from 55 to 58 beats a minute are not uncommon, and occasionally the pulse rate falls suddenly to from 20 to 40 beats, so that one may speak of a pulse crisis. This crisis may occur several days after the temperature has reached the normal point; in other cases it falls more gradually. Especially notable at this stage is the instability of the heart's action; daily variations of 20 and more beats may occur. In other cases the pulse rate remains high after the temperature has become normal. Such irregularities may be transient, no further symptoms of circulatory derangement following, but when marked they are usually the precursors of more serious manifestations. The pulse after dropping to normal with the temperature may remain there for several days and then suddenly rise to 130 or more, persisting at this rate with wide daily variations for several weeks. This rise, in what Schmoltz terms the tertiary period, always indicates some cardiac lesion.

During the early stages of the disease the first heart sounds often show some impurity or a systolic murmur, which commonly vanishes in a few days, but in some cases becomes more marked as the temperature falls, while other symptoms arise which leave no doubt as to the presence of a heart lesion. More often murmur develops at the end of the first or during the second stage; not infrequently they appear later. Their character is various, at times blowing, at times harsh and humming; no diagnostic importance can be attached to these differences. They are almost always systolic in time, sometimes louder at the apex, sometimes at the base. Such murmurs are usually accompanied by an accentuated second pulmonic sound. The second pulmonic may be accentuated before the development of a murmur or without a murmur; in these cases it is frequently associated with an irregular or a rapid pulse. Such changes may be present with no alteration in the area of cardiac dulness or in the position of the apex beat, but frequently there is enlargement to the left and often also to the right and upward, while the point of maximum impulse moves outward. In 14 per cent. of his cases Schmoltz observed an increase in the area of dulness; in some of these no murmur developed. It is important to note that such dilatation may be deferred to the period of convalescence, when it may follow suddenly some unusual exertion. Schmoltz finds that dilatation sets in most frequently toward the end of or after the febrile period, sometimes after a considerable length of time. While irregularity of the pulse is usual in these cases, it may be absent, as in diphtheria, even in cases with most marked dilatation.

Practically no subjective symptoms accompany these lesions as long as the child remains in bed, though there may be palpitation and a little dyspnoea. The temperature remains normal or is but slightly elevated. Cardiac complications are not much more frequent after the severer attacks of scarlet fever with marked involvement of the throat than after milder cases, and some of the gravest cardiac lesions follow very mild attacks, with uncomplicated convalescence. As rheumatoid pains are very common in scarlet fever, Heubner has referred both joint and heart lesions to a rheumatic infection. Schmoltz, on the other hand, finds that cardiac lesions are no more frequent among the cases with arthritic pain than in instances without these symptoms. He believes the two complications bear no further relation to one another than that of having a common cause. Hearts damaged before the onset of the infection bear the brunt of the attack well. Of 27 cases showing, on admission, a slight mitral insufficiency, 17 passed through the illness without apparent damage to the heart; in 5 cases there was transient arrhythmia or an unusually rapid pulse in the latter part of the disease; in 3 slight dilatation was made out.

The ultimate outcome of cases with these cardiac manifestations varies. In a large proportion all the symptoms disappear. In 29 cases of this series, however, changes persisted on discharge. In 19 of these cases and 5 more which, on discharge, showed no abnormalities, he was able to observe subsequently. In 18 abnormal cardiac conditions were found. In 16 signs of a definite mitral insufficiency, systolic murmur, accentuated second pulmonic, and in some fairly well-marked cardiac enlargement. In the other 2 cases a systolic murmur alone was found. In 6 cases the heart seemed normal. Of the 18 affected, 5 had become worse after discharge. These displayed during their illness some circu-

latory disturbance, but on discharge were quite free from unusual signs. Three cases had improved after discharge, the symptoms then present having cleared up. Of the 16 cases with persisting cardiac lesions in 13 over six months had elapsed since the attack, in 4 one year, and in 2 over five years.

These heart affections were formerly all referred to an endocarditis, but since Romberg's paper the importance of the myocardial changes has been more generally recognized. Endocarditis is a very rare incident in scarlet fever. In a review of 30 autopsies the author could find only 3 showing slight changes in the valves. Myocarditis is, on the other hand, very common, and there can be little doubt that most of the symptoms are referable to this lesion. Why the signs of a mitral insufficiency should so frequently persist may be variously explained. It is now well known that a relative insufficiency, lasting indefinitely, may depend upon changes in the heart muscle.

The heart in scarlet fever should be carefully watched, not only during the disease, but also in convalescence. Grave results may follow too early strain. When cardiac complications arise, the one important point in treatment is to insist upon prolonged rest in bed.

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**Diseases Due to Trypanosomes.**—ROBERT KOCH (*Deutsche med. Wochenschrift*, 1904, xxx. p., 1705) states that since the discovery of the malarial parasite by Laveran and pyrosoma bigeminum by Theobald Smith, recognition of the importance of the protozoa has spread rapidly. The appreciation of the important role of one especially interesting group of parasites, the trypanosomes, which were shown by Bruce in 1895 to be the cause of the tsetse disease in animals, is a result of investigations of the past few years. The trypanosomes belong to the group of flagellates, and in fresh blood preparations move about with great activity. They are two or three times longer than a red corpuscle, have a long flagellum on the fore end, and are surrounded by a loose, undulating membrane. Stained by the Romanowsky method, they show a large red nucleus and an intensely red centrosome situated near the hinder end, from which a red line runs along the undulating membrane, ending in the red tail. The body is blue and without pigment.

Trypanosome infections have many features in common with malaria. They may run an acute course, but are more usually chronic and sometimes drawn out for years; they cause irregular fever, often with longer or shorter remissions, anæmia, emaciation, loss of strength, localized œdema, enlargement of lymph glands and spleen.

The best known of these infections is the tsetse disease, due to trypanosoma Brucei, and transmitted by the bite of glossina morsitans, the tsetse fly. The disease was first observed in the valleys of the Limpopo and Zambezi, but is now known to extend on the east coast of Africa from Natal to Somaliland and on the west coast up to Senegal, through the Congo basin about Lake Tchad, and upward to Southern Algeria. Nearly all domestic animals are susceptible; the organism is very pathogenic for laboratory animals.

Similar to tsetse disease is surra and the mal de Caderas. Surra is a disease affecting horses and camels in Asia; in some regions it attacks the cattle. It extends from Persia to Indo-China, and in recent years has been conveyed to the Philippines, to Java, to Mauritius, and to

Abyssinia. Mal de Caderas is prevalent among horses in South America, extending from Argentina to the Amazon. Both diseases are conveyed by a fly of the variety of *Stomoxys*, and the trypanosomes causing them are indistinguishable in their morphology and pathogenicity from the tsetse trypanosome.

These observations became of special interest when Dutton, in 1901, found trypanosomes in the blood of a native of Gambia suffering from what was thought to be malaria. Confirmation of his report soon arrived from all sides, and its significance was fully realized when Bruce, in 1903, established the etiological relation of trypanosomes to the sleeping sickness. This disease was known in the beginning of the last century. It was observed principally among the negro slaves on the west coast of Africa and frequently transported to the West Indies, where it was noted that the disease might occur in slaves from five to eight years after leaving Africa. It never took root in the Indies, evidently, from our present knowledge, because there were no flies to carry it. At that time the affected area in Africa reached from Senegal to the boundary of Angola, but recently it has been carried to the Congo basin, and from there, in 1896, to Uganda. Here the disease seems to have found especially favorable conditions, about 200,000 people having succumbed to it in a few years. Bruce, among 80 apparently healthy natives, found that 23 showed trypanosomes in the blood. The symptoms of human trypanosomiasis are similar to those observed in animals. Sometimes there are no symptoms for a long period after infection; then irregular fever, anæmia, loss of strength, emaciation, local oedema, erythema, glandular enlargements (particularly of the back of the neck), and enlargement of the spleen.

The blood infection—trypanosomiasis—and the sleeping sickness were at first regarded as different diseases, but when it was shown that patients with the sleeping sickness also had trypanosomes in their blood, and that those with trypanosomiasis frequently developed the sleeping sickness, it became evident that the nervous symptoms were due merely to a special localization of the general infection. The organisms are carried by the fly *glossina palpalis* and are, in all respects, analogous to those discovered in the tsetse disease, surra, and mal de Caderas.

The trypanosomes obtained from cattle in South Africa and described by Theiler in 1902 are easily distinguished, in being from two to three times longer than those from other sources. They are also peculiar in being pathogenic for cattle alone. The disease, although widespread, is mild, and not more than 5 per cent. of affected animals die. The rat trypanosome is also a definite variety. It is characterized morphologically by the drawn-out and pointed character of the hinder end and by the fact that the centrosome is nearer the centre. The infected animals do not appear ill, and the organism cannot be transferred to other species.

The trypanosomes of cattle and rats are distinguished by constant qualities which are lacking in the organisms of tsetse, surra, mal de Caderas, and the sleeping sickness. The former have a characteristic morphology, a uniform virulence, and a single host, qualities pointing to an adaptation to surroundings enjoyed through many generations; the latter are morphologically variable, show a wide range of virulence, and can be transferred to numerous species, qualities pointing to a recent

invasion and an incomplete adaptation to new surroundings. These qualities are well illustrated in the tsetse trypanosome. It is relatively small and has a broad blunt end when grown in rats, cattle, and dogs, while in horses it is larger, the hinder end being drawn out and tapering, so that they resemble somewhat the rat trypanosomes. Of animals passing through a tsetse region, one may acquire an extremely virulent infection and another a very mild infection; and the respective organisms may retain these characters when inoculated into other animals. The virulence of an organism may, however, be greatly increased by successive passages through animals, and it was noted that dogs who resisted inoculation with a trypanosome of low virulence would succumb to the same strain after it had been passed through a number of other dogs. It is also possible by varying the animals to reduce the virulence. While the tsetse trypanosome can be successfully inoculated into nearly all mammals, one meets with varieties which are more virulent for cattle, others for camels, others for horses, etc., indicating a tendency of the parasites to adapt themselves to their host; and such a tendency may, through many generations, become a fixed character.

It has been shown that animals having withstood an infection with a trypanosome of low virulence acquire an immunity against subsequent inoculations with more virulent strains. This fact might suggest a ready means of preventing the disease. Experience, however, has shown that trypanosomes may live in these immunized animals for many years after the protective inoculation, and result in the end in a more fecund source of infection. All investigators consider that antelopes and buffaloes who harbor the organism without suffering themselves are the chief factors in the spread of the disease. Too little is known of the habits and life history of the flies of the *Stomoxys* and *Tabanus* species to direct an active campaign against them, but it has been repeatedly noted that with the destruction or emigration of the wild animals both the tsetse fly and the tsetse disease disappear. Drugs have proved of some benefit in human trypanosomiasis, and the results permit the hope that much more effective ones will be discovered.

At present the most fruitful method of attacking the disease is by prevention, and the necessary steps are very simple. All infected animals should be killed, and those suspected carefully isolated. It is important to examine even healthy animals, as it has been found that, without symptoms, they may harbor the organisms for years. The value of these precautions is illustrated in the respective experiences of Java and Mauritius. Surra was brought from India to both countries by cattle. In Java the disease was early recognized and careful isolation practised, so that little damage was done. In Mauritius it was recognized late, and even after recognition little effort made to check it, with the result that in two years all the horses and mules and nearly all the cattle died.

[Those interested in the subject of trypanosomiasis are referred to the admirable work of Laveran and Mesnil, *Trypanosomes et Trypanosomiasis*, 8°, Paris (Masson), 1904, and that of Musgrave and Clegg, *Trypanosoma and Trypanosomiasis, with Special Reference to Surra in the Philippine Islands*, 1903, No. 5, Department of the Interior, Bureau of Government Laboratories, Biological Laboratory, 8°, Manila.—W. S. T.]

## THERAPEUTICS.

UNDER THE CHARGE OF

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**Sodium Salicylate in Exophthalmic Goitre.**—DR. G. JOUSSEMET states that while this valuable treatment of exophthalmic goitre is by no means new it seems to be little known. It is not applicable to all forms of the disease, but in the pure form, with or without thyroid enlargement, it will be found to be of worth. Treatment of the general condition is a necessary adjuvant of the salicylate. A drachm or more per day may be given in the cures of rapid course, but in those of slower evolution smaller dosage will suffice. The objections to the treatment, since it must be in many cases continued for a year or more, are the possibility of injuring the kidneys—making frequent urine examination necessary—disturbing the digestion and the unpleasant taste of the drug. Sodium bicarbonate may be given as an adjuvant, but by far the best method of administration is to give it largely diluted in water or milk. Some patients who bear the drug particularly ill will tolerate it when given mixed with a large quantity of vichy. Untoward symptoms may necessitate intermission of the treatment. The long continuance of the treatment is its greatest disadvantage, but this drawback exists in other methods as well.—*Revue française de médecine et de chirurgie*, 1904, No. 34, p. 811.

**The Action of the X-rays upon Leukæmic Blood.**—MM. AUBERTIN and BEAUJARD conclude an article upon this subject with the following *résumé*: Radiotherapy provokes in myelogenous leukæmia a diminution of the number of the leukocytes, but this diminution is not regularly progressive. Each application of the rays is followed by a sudden and considerable increase of the white cells, but following this there is a slow but progressive diminution in their number. At first the increase in the cells is almost immediate, but as the organism becomes used to the treatment it becomes more slow. Finally the increase becomes imperceptible and only the diminution is noticeable. The increase in leukocytes involves both the myelocytes and the polynuclear cells, and occurs as a result of a rapid overproduction and maturation—which is an improbable theory—or, as a result of an unknown action of the x-ray upon the splenic tissue, causing an emigration of adult leukocytes just as they normally emigrate from the bone-marrow. In fine, the first effects of radiotherapy are these profound

changes in the blood taking place before the spleen has begun to appreciably diminish in volume.—*La presse médicale*, 1904, No. 67, p. 533.

**Bioson.**—DR. M. HEIM reports on this albuminate of iron-lecithin combination as follows: Bioson combines the nutrient and blood-enriching properties of iron and the nerve-strengthening action of lecithin; it may be administered for long periods without disturbing digestion; it is well borne in acute febrile conditions; it increases body weight; it increases the appetite; it augments the hæmoglobin and the number of red blood cells; it acts well in exhausting diseases, and is recommended by its comparative cheapness.—*Berliner klinische Wochenschrift*, 1904, No. 22, p. 593.

**Thiocol in Tuberculous Enteritis.**—DR. A. L. VIGNON cites a case of pulmonary tuberculosis in which this drug was used with excellent effect. From the beginning it caused an increase of appetite, a cessation of the night-sweats, a tendency toward healing of the lesions, an improvement of the general condition, and an increase in body weight. When the drug was stopped the symptoms reappeared and in addition the infection spread to the intestine. Thiocol was again prescribed and the symptoms immediately became less distressing. The enteritis and bronchitis disappeared, the appetite returned, and the patient's weight began to increase. Observation of this case seems to show that thiocol acts indirectly upon the pulmonary lesions by causing a remarkable amelioration of the patient's general state. The author believes this agent to be the drug of choice in the treatment of tuberculosis, since in every case it stimulates appetite, digestion and assimilation, and in the case cited, at least, it caused a spontaneous arrest of the symptoms of the enteritis, and consequently seems to have an antiseptic action upon the intestinal tract.—*Le progrès médical*, 1904, No. 36, p. 152.

**Rectal Feeding, Especially in Gastric Ulcer.**—DR. C. KLEINEBERGER, after investigating Lenharz's statement that blood deterioration follows feeding *per rectum*, and that the anæmia secondary to the hæmatemesis is augmented, concludes that in the course of rectal alimentation the composition of the blood is not affected, nor is there deterioration of the heart's action. The hæmoglobin content of the blood is not lowered unless further vomiting of blood takes place. The author's treatment was as follows: Complete cessation of feeding by mouth for from nine to twenty days after hemorrhage; rest in bed for at least three weeks; two or three nutritive enemata daily, consisting of from 6 to 12 ounces of milk, 2 or 3 eggs, a coffeespoonful of salt, and a dessert-spoonful each of sugar and plasmon. In patients whose rectum was irritable, a few drops of laudanum were added. An hour before the feeding the bowel was irrigated with a quart of water.—*Therapie der Gegenwart*, 1904, No. 5, p. 197.

**The Treatment of Coma.**—DR. FIESSINGER finds that in meningeal affections complicated by coma lumbar puncture is attended with good results. In coma due to cerebral hemorrhage he employs the usual methods, and when he bleeds does so with great care. As a



prophylactic measure against the coma of grip or acute mania he advises warm baths lasting in the former affection fifteen minutes to three hours, in the latter one to two hours, morning and evening. In the coma of sunstroke he prescribes the application of ice-bags to the head and venesection. In coma brought on by intense cold he rubs vigorously with snow or cold water and gives cold drinks. Hot drinks are indicated after consciousness has been restored. Diabetic coma is to be treated by prophylactic measures. Coma occurring in the course of the infectious diseases is variously treated. In rheumatism intravenous injections of sodium salicylate and cold baths are recommended. In other infections hydrotherapy by means of cold or warm baths meets the indication.—*Journal des praticiens*, 1904, No. 28, p. 437.

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**Subcutaneous Injections of Air in Neuralgias.**—DRS. MONGOUR and CARLES employ the following technique: Under antiseptic precautions and with care not to draw even a drop of blood, a needle is inserted into the intramuscular planes of the chosen site, and a bicycle pump or bulb of a Pacquelin cautery being attached, the desired quantity of air is injected. This varies from one-half pint to one pint, depending on the sensations of the patient. The injection of the air has in some cases an immediate anæsthetic effect. Light massage should follow the procedure, and it is well to repeat this for a few days until the crepitation due to the air has disappeared. Of 25 cases of sciatica treated by this method, 13 were cured and but 2 were unimproved. The explanation that this method of treatment acts by mechanical pressure upon the nerve endings seems to be the true one, since the massage after injection increases the good effect of the procedure, and since the pain reappeared to some extent as the air is absorbed, only to disappear after a renewal of the treatment. Consequently air is as effectual an injection as any of the other gases with which experiments have been made. The treatment is applicable to various forms of neuralgia which resist other methods.—*Journal de médecine de Bordeaux*, 1904, No. 35, p. 633.

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**The Treatment of Whooping-cough.**—DR. STEPP believes that fluoroform has a specific action in pertussis. He has obtained in 20 instances what he considers a cure, in that the patients after from six to thirty-seven days of treatment were permanently relieved of the characteristic cough. Fluoroform may be given to patients of all ages without regard to their condition in other respects, which is a strong point in its favor. The paroxysms are diminished in force and frequency from the first day of its administration. The drug is given in 2 to 2.5 per cent. aqueous solution, which possesses no taste or odor, and has the single disadvantage of causing slight pharyngeal irritation as it is swallowed. To young infants a coffeespoonful may be given every hour; to older children, from a teaspoonful to a dessertspoonful.—*Therapeutische Monatshefte*, 1904, No. 11, p. 549.

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**Arsenic and Creosote Treatment of Pulmonary Tuberculosis Compared.**—DR. DUCOT contrasts sodium cacodylate given hypodermically with thiocol in pulmonary tuberculosis as follows: The use of the cacodylate increases the appetite and the body weight; these effects are temporary

and due to a direct action of the drug upon the anatomical elements of the body. The toxicity of the cacodylate forbids its continued use, and the drug is contraindicated in fever and hæmoptysis and does not seem to influence the pulmonary lesions. In the author's experience, on the other hand, thiocol is without poisonous effects and does not disturb the digestion. It is a stomachic and an intestinal antiseptic, it increases the appetite and the bodily vigor, it reduces fever, and causes the functional symptoms to disappear, and, more than all these, it tends to cicatrize the pulmonary lesions. Its only disadvantage is that it tends, on account of its ability to produce congestion, to cause the expectoration of bloody sputum. With the cacodylate we get an antianæmic effect; in thiocol we have a therapeutic agent of true antibacillary power.—*Gazette médicale de Paris*, 1904, No. 47, p. 528.

**Landerer's Treatment of Pulmonary Tuberculosis.**—DR. F. SCHRAGE describes the mode of action of this method of treatment as follows: Its objects are (1) to produce a general leukocytosis; (2) to produce an aseptic inflammation about the tuberculous foci. In 1893 Landerer introduced the treatment by hetol, an easily soluble preparation of sodium cinnamate. The treatment is most applicable to incipient and uncomplicated cases—*i. e.*, patients displaying no rise of temperature and with slight destruction of lung tissue. On the other hand, apyretic cases with small cavities are also amenable. Rapidly progressing and advanced cases should be treated only in sanatoria. In properly selected cases the cinnamate seems to have a true curative action; following the injections the evening rise of temperature disappears, the night-sweats are quickly stopped, and the weight increases. The rales disappear; the sputum is less and becomes free from bacilli. The efficacy of this treatment should, in the author's opinion, encourage us to make the diagnosis as early in the disease as possible.—*Münchener medizinische Wochenschrift*, 1904, No. 44, p. 1954.

**Eumydrin, a New Drug for Diminishing Sweating.**—DR. BERNARD ENGLÄNDER states that this agent, which is methylatropine nitrate, is an excellent preventive of excessive sweating, especially in pulmonary tuberculosis. It is a white powder, moderately soluble in water, and may be given in doses of from 0.015 to 0.0375 grains. Most patients bear the drug well, and there is seldom any complaint of gastric distress, ringing in the ears, dryness of the mouth, palpitation, or insomnia. Increased intestinal peristalsis and pupillary dilatation may occur. In addition to checking the perspiration in tuberculous conditions, the general condition of the patient is improved, the appetite is increased, and his bodily vigor is augmented.—*Weiner klinisch-therapeutische Wochenschrift*, 1904, No. 48, p. 1261.

**The Treatment of Glycosuria and Diabetes.**—M. M. HUCHARD and FIESSINGER consider the arsenical mineral waters useful in pancreatic diabetes, with antipyrin or aspirin as adjuvants. Nervous diabetes may respond to the use of potassium bromide in dosage of 1 drachm daily or valerian in the form of the extract. In all forms of the disease the diet is the same. Potatoes (4 to 5 ounces per day) are allowable. The various forms of diabetic bread, except possibly the aleuronat bread of Ebstein, all have their disadvantages. Milk diet may be

employed in hepatic diabetes with an enlarged liver, and this regimen is necessary if the condition is complicated with intestinal nephritis. The patient should drink considerable amounts of the infusions of quassia or cinchona; only a little wine should be permitted; beer, cider, and sweet wines are to be interdicted. Fruits, preferably apples and peaches, may be eaten in small quantity. Starchy and sugary foods must be suppressed. Meats except liver may be allowed in moderate amount. Eggs are excellent, as also are all the green vegetables. With regard to drugs, antipyrin, aspirin, and arsenic are the most useful. The first should be given in doses of 20 grains in two powders before the principal meal for about a week, and followed by sodium arsenate  $\frac{1}{20}$  to  $\frac{1}{15}$  of a grain. If the glycosuria is marked and the digestion good, a pill containing the latter drug and codeine may be given. To this pill valerian may be added to lessen the polyuria. Moderate exercise, warm baths, and avoidance of emotional disturbance are to be advised.—*Journal des praticiens*, 1904, No. 43, p. 691.

**Resorcin in Sycosis.**—M. G. BELGODÈRE reports upon the results attained by the use of a spray of 1 per cent. aqueous solution of resorcin, and attributes excellent results to its employment. The solution is used in an atomizer, the nozzle of which is held eight to ten inches from the affected part, and is employed for from ten to twenty minutes daily. The spray passes easily through the hair and penetrates to the skin. It is often useless to shave the region or to epilate in the milder cases, and it is unnecessary to apply wet dressings of the solution, except in severe cases where they may be applied during the night. In the author's experience, under this treatment, the redness decreases, induration disappears, and the tissues regain their normal condition, the cure necessitating a period of from two to seventeen weeks.—*La semaine médicale*, 1904, No. 48, p. 392.

## OBSTETRICS.

UNDER THE CHARGE OF

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**Tubal Gestation.**—In the *Journal of Obstetrics of the British Empire*, February, 1905, BERKELEY and BONNEY contribute a paper entitled "Tubal Gestation."

They have examined 18 specimens of early tubal pregnancy, the period varying from nineteen to thirty days. They found that early tubal gestation is entirely intramural. In no point did the gestation sac communicate with the lumen of the tube.

So far as the formation of a decidua was concerned in the specimens examined, there was an absence of connective-tissue reaction to the

invading ovum. They did not find decidua cells in the ovary of the opposite tube or the peritoneum.

Their specimens showed that the ovum travels toward that part of the tube where the nutrition and the vascular supply is most copious. In most cases implantation occurred in the attacked half of the tube wall.

The writers believe that the cells previously described as decidua serotina are identical with the trophoblast of the early gestation sac. The splitting of the circular from the longitudinal muscle coat was very striking in the specimens studied by the writers.

In these specimens synechium was found in masses on free surfaces in contact with maternal blood. Fetal tissue invaded the walls of the bloodvessels from without, or sometimes replaced part of the vessel wall. In the latter the tissue probably made its way along the lymphatics.

The rupture of the primary gestation sac may be brought about by mechanical causes or by the destructive action of the trophoblast.

Another factor is bleeding from maternal vessels into the gestation sac, causing a sudden rise in tension, rupturing the sac wall already weakened by the action of the trophoblast. This hemorrhage either occurs into the intervillous space containing blood or into the space between the amnion and chorion. In most of the cases examined there was undoubted evidence of bleeding into the sac.

Rupture usually takes place in one of three directions: first, the gestation sac may rupture through the tube into the peritoneum or into the broad ligament; this occurs most frequently at the isthmus of the tube, and results from the destructive action of the trophoblast alone.

The gestation sac may also rupture into the lumen of the tube; this constitutes tubal abortion.

The gestation sac may also rupture within the wall of the tube, constituting intramural rupture.

In these cases the longitudinal muscle coat is split off from the circular muscle coat and blood extravasates between these two. A mass forms which appears externally as a sausage-shaped enlargement of the tube.

These cases are mistaken for hæmatosalpinx, which they resemble.

This blood sac frequently bursts, and the contents then escape into the peritoneal cavity, broad ligament, or lumen of the tube. The first is the most common perforation, which is often closed temporarily by blood clot. The blood sac often bursts into the tube itself, and blood may pass thus into the peritoneum or may accumulate into the tube.

Intramural rupture is more common in the ampulla of the tube than in the isthmus.

Combined varieties of the rupture of the gestation sac, also, frequently occur.

So far as the causation of extrauterine pregnancy is concerned, the examination of these specimens gave no information.

There was no sign of pre-existing salpingitis, nor were there abnormalities in the tubes.

In 3 pregnant tubes of less than a month's duration, the corpus luteum was found in the ovary of the opposite side in 2 cases, and in the ovary of the same side in 1 case.

**An Investigation into the Causation of Puerperal Infections.**—FOULERTON and BONNEY (*Journal of Obstetrics of the British Empire*, February, 1905) give the results of their investigations in 96 cases, in which 12 had a normal puerperal period, 54 had either miscarriage or labor at term, followed by fever, and 30 cases had cervicitis in non-pregnant conditions.

Fourteen of these patients were in a lying-in hospital, while the remainder came from out-patient departments and private practice.

Material for examination was obtained by using a glass tube, the shape and dimensions of an intrauterine douché tube. This served for a sheath for a wire with a plug of sterilized cotton-wool at its extremity. The upper end of the glass tube was covered with a cap of cotton-wool. After sterilization the cap of cotton-wool was dipped in a mixture of melted paraffin and thymol. After the glass tube had been introduced into the lower part of the uterus, the cotton-wool cap was withdrawn by a piece of string, the wire carrying the sterilized plug of wool was pushed up to the fundus, and a sample of the uterine contents was obtained. The cultures were then made.

These investigations are especially valuable, because they represent the average case seen by physicians, both in hospitals and in private houses.

In the normal puerperal period the cavity of the uterus was sterile.

In 54 cases there was fever in the puerperal period; 48 of these were after labor at full term, and 6 after primary labor or miscarriage.

In 14 of these cases there were severe symptoms terminating in death, and in all of these bacteria were found within the uterus.

In 26 cases there were severe symptoms terminating in recovery, and in these bacteria were found in the uterus in 21 cases.

In 14 cases there was fever not exceeding  $102^{\circ}$ , and in these 14 the uterus was sterile in 10, and bacteria were present in 4.

Regarding the kind of germs in fatal cases, the bacteria which seemed most abundant and potent were streptococci and the micrococcus of pneumonia. In many cases these bacteria were associated with others.

In the second group of cases, with severe symptoms terminating in recovery, streptococci predominated, but the micrococcus of pneumonia was also found. It seemed as frequent and as potent as the colon bacillus in the last group of cases, in which the fever was slight and the uterus was sterile in 10 out of 14. In the 4 cases in which germs were found within the uterus, the streptococcus was absent. The bacteria present were the staphylococcus pyogenes albus and bacillus coli communis.

In non-pregnant women suffering from cervical inflammation, 30 in number, cultures of bacteria were obtained in 16. These were the staphylococcus pyogenes aureus, micrococcus of gonorrhœa, and the bacillus coli communis.

The general result of the bacteriological work in these cases was that streptococci were present in the uterus in 25 out of 39 cases of infection in which cultures from the uterus were taken.

In 17 cases where the contents of the uterus were apparently sterile, streptococci were found in the vagina in 2 cases.

In severe fever, streptococci were present in the uterus in 25 out of 40, and in the vaginal secretion in 2 out of 5:

In 15 cases in which the contents of the uterus were sterile, a marked proportion were primiparæ, with considerable lacerations of the cervix

or perineum. A noticeable feature was the absence of the micrococci of gonorrhœa and anærobic organisms.

In non-pregnant cases, streptococci were not found. Another noteworthy fact was the apparent absence of the bacillus coli communis in cases of primary infection.

The writers believe that puerperal fever may be caused by primary infection of lacerations in the vaginal walls or perineum, with sometimes secondary infections of the uterus. There may also be primary infections of the contents of the uterus or at the placental site.

So far as the treatment is concerned, the writers believe that when bacteriological proof of the nature of the infection is wanting, a case of puerperal fever should be treated as being due to streptococci infection.

Active ennetting of the uterus in puerperal infection is not advisable. They believe that the best treatment for streptococci infection is the administration of serum, with thorough cleansing of the uterus cavity, followed by intrauterine douches.

In cases of streptococci infection the fever is often transient, subsiding within forty-eight hours, without treatment.

Antogenetic infection is probably, sometimes, the cause of fever, but the use of vaginal douching before labor is not advisable.

In the cases reported the temperature rose with severe symptoms when bacteria entered the uterus. In cases having severe lacerations of the cervix or perineum, the symptoms were much less severe, and the temperature did not rise above 102°.

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**Artificial Termination of Pregnancy by the Use of Bougies.**—JACOBY (*Archiv f. Gyn.*, 1904, Bd. lxxiv., Heft 2) gives the results of 228 cases of induced labor by bougies in the Mannheim clinic.

There were 81 cases of contracted pelvis. In these the fetal mortality varied directly with the degree of pelvic contraction and with the shortness of gestation. Two facts are clearly brought out: first, that labor should not be induced in contracted pelvis in the interest of the child before thirty-five weeks of gestation, and, second, the fact that in these cases operative treatment during labor largely increases fetal mortality.

As to the percentage of children surviving labor in contracted pelvis, it is stated as 65. Evidently the results of induced labor in contracted pelvis, so far as the children go, are much inferior to those of Cæsarean section.

So far as the mothers are concerned, in 50 cases, 3 died; 1 from hemorrhage, and 2 from septic infection.

This causes a maternal mortality, in 50 cases, of 6 per cent.

In 57 cases labor was induced by bougies for maternal disease, for eclampsia, nephritis, heart disease, mental disease, pernicious nausea, uterine displacement, polyhydramnios, and fetal death. Bougies alone were used and bags were not employed. The average time in which bougies remained in the uterus was twenty-four hours.

In a case of polyhydramnios, a bougie was left fifty-four hours in the uterus. The patient died after labor.

If those cases were removed in which the maternal disease influenced largely the condition, the morbidity rate would be between 8 per cent. and 9 per cent.

**Hemorrhages in Eclampsia.**—LOBENSTINE (THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, February, 1905), at the Sloane Maternity Hospital, found, in 12,000 deliveries, 152 cases of eclampsia. Among these 7 had hemorrhages and 5 occurred during the past two years.

In Case 1, on the second day after delivery, the patient was delirious, without convulsions, but had severe abdominal pain and distention. There was great tenderness over the liver. Toward the middle of the day the patient began to vomit coffee-ground material, speedily followed by death.

In Case 2, on the third day of the puerperal period jaundice, pain and tenderness over the liver and vomiting of coffee-ground material occurred. This continued until the fifth day of the puerperal period, after which the patient speedily improved, and finally recovered.

In Case 3, a white primipara, the same symptoms began soon after delivery. The patient died on the fourth day of the puerperal period.

In Case 4 the patient was admitted in an unconscious condition, having had several convulsions. On the first day of the puerperal period she became jaundiced, with distended and painful abdomen and a very high leukocytosis. Her temperature rose to 102.8°. On the second day of the puerperal period her condition suddenly grew much worse. There was marked tenderness over the liver, bloody vomit, and tarry stools. In the early afternoon she vomited bright-red blood and soon after died.

Case 5 was a woman in the second pregnancy, six and a half months advanced, who came into the hospital complaining of headache and dizziness. The uterus was emptied, and on the first day of the puerperal period coffee-ground vomiting, with abdominal pain and distention, occurred. On the second day the patient was delirious, jaundiced, vomited coffee-ground material, and had subcutaneous hemorrhage. She vomited bright-red blood at times, gradually became comatose, had frequent, loose, dark, tarry stools, and died on the eleventh day.

In Case 6 the patient passed through nine days of the same symptoms, and finally made a gradual recovery. The mortality of these cases was 70 per cent. There is no record of autopsies performed upon any one of them, although autopsies are quoted as reported by other observers. Clinically, the significant fact about these cases was the very evident profound toxicity and the severe involvement of the liver. The significance of hemorrhage after eclampsia may be inferred from the fact that the mortality of the general series of eclampsia cases during the past four years at the Sloane Maternity Hospital was 17 per cent., while in the cases associated with hemorrhage the mortality was 70 per cent.

The writer has several times seen hemorrhage in toxæmia and eclampsia. Recently he had occasion to dilate the uterus by Bossi's dilator and terminate an early pregnancy in eclampsia. The patient did well for the first week, the urine becoming almost normal and the temperature remaining normal. At the end of the first week she had a severe uterine hemorrhage. Symptoms of rapid disintegration of the blood developed, and she died within twelve hours of the occurrence of the hemorrhage.

In infants born from eclamptic mothers, hemorrhage is not infrequently observed about the umbilicus or beneath the skin. Dark, tarry stools and profound jaundice accompany these phenomena in fatal cases.

**Concerning Uterine Structure.**—STEPHENSON (*Scottish Medical and Surgical Journal*, January, 1905) draws attention to what he considers an erroneous idea concerning the arrangement of the tissues of the uterus. He believes that the common teaching that the muscle of the uterus occurs in distinct layers and that these layers can be demonstrated by dissection and found to extend in definite directions is to be rejected.

He quotes other observers, and adds his own investigations to prove that the walls of the uterus are arranged first upon a connective-tissue framework. The meshes of this framework are flattened in a plane parallel with the surface, being filled in with muscular tissue, which appears as plates and not as bundles of fibres when the uterine wall is studied in sections. This lamellate arrangement allows one stratum to move upon another or several to join in a sliding movement in the same direction.

Regarding the lower uterine segment, he believes it is not elastic only, but that it has sufficient muscular tissue to exercise some force. The thickening when the uterus is empty is on the inner side, and there is evidently a difference in behavior between the outer and inner portions of the walls. While he believes that the cervix remains such throughout pregnancy and parturition, he also believes that there is an external muscular wall, uniform in structure, continuous throughout the uterus, and prolonged into the wall of the vagina. He believes that the connective tissue of the cervix is an extension of that found in the body of the uterus, and that it exists in the form of a cone, the base of which is at the vaginal portion of the cervix, the tissue growing thin as it passes upward to the internal os.

During labor the lamellate construction of the uterus appears throughout its whole muscular tissue. When retraction has taken place, this lamellate appearance is fairly well maintained in the outer subperitoneal portion, which is undisturbed in the lower uterine segment, and so long as the placenta is attached it remains at the placental site. From the retraction ring upward the lamellæ of the inner portion are crumpled into a confused mass, where islets of muscle, surrounded by connective tissue, can be demonstrated.

The ovum is retained within the uterus, not by the action of sphincter fibres, but because the ovum is an integral part of the pregnant uterus, and the shape of the womb and its structure further its retention. During pregnancy the cavity of the uterus is kept closed by the cervix, which resists strain brought to bear upon it. When the cervix softens and the womb opens, the ovum may be expelled.

As regards the action of the uterus in labor, he believes that the preliminary softening and shortening of the cervix, and even its disappearance, should be considered a process of dehiscence. This botanical term, originally applied to changes in the connection between ripe fruit and the parent stem, accurately describes this process in the uterus.

On the contrary, in labor the whole uterine muscle is thrown into action, steadily progressing with increasing energy, often through hours. On the other hand, the process of dehiscence may extend over days and weeks.



## GYNECOLOGY.

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UNDER THE CHARGE OF

HENRY C. COE, M.D.,  
OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

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**Vaginal Ovariectomy during Pregnancy.**—MAINZER (*Zentralblatt f. Gynäkologie*, No. 48, 1904) reports the following cases:

Case I. The patient, aged twenty-five years, who was in the fourth month of pregnancy, had an ovarian dermoid the size of the fist. The patient had a normal convalescence, sitting up on the tenth day. The pregnancy was not interrupted.

Case II. A dermoid, the same size as in the former case, was removed per vaginam from a patient two months pregnant. She aborted on the twelfth day after operation, which was attributed to the presence of a large tampon that had been inserted for drainage.

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**Influence of Castration on Metabolism.**—ZUNTZ (*Zentralblatt f. Gynäkologie*, 1904, No. 48), from experiments in 4 cases of oöphorectomy, found that removal of the ovaries caused little or no change in metabolism, nor was any marked increase noted after the administration of oöphorin. This result is the reverse of that observed by Lowry and Richter in their experiments upon dogs, although the same quantities of the drug were administered. The writer infers that there may be a difference in the tablets, whether prepared from the corpus luteum or from the stroma. It is possible also that the age of the ovaries makes some difference in the effect of the preparation.

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**Migration of the Ovum.**—BURCKHARD (*Zeitschrift f. Geb. u. Gyn.*, Band lii., Heft 3) denies the possibility of internal migration because of the size of the impregnated ovum and the direction of the ciliary motion. He is also skeptical with regard to the occurrence of external migration on account of the wide separation of the distal ends of the tubes, and the tendency of the peristaltic movements of the intestines to carry the ovum in a different direction. However, in case both tubes are prolapsed into Douglas' pouch their fimbriated ends may lie so close together that external migration is possible.

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**Closure of the Tubes.**—OPITZ (*Zeitschrift f. Geb. u. Gyn.*, Band lii., Heft 3) calls attention to the fact that there is a layer of loose connective tissue beneath the peritoneal covering of the tube, the peritoneum being closely attached behind the fimbriæ so as to form a ring at this point. When the tube becomes swollen from inflammation the fimbriæ are drawn into the distal opening, which is subsequently closed. The more the tube enlarges the more the fimbriæ are drawn inward until their peritoneal coats adhere, after which fluid accumulates in the tube.

**Conservative Myomectomy.**—HENKEL (*Zeitschrift f. Geb. u. Gyn.*, Band lii., Heft 3) reports 40 cases, 3 patients subsequently becoming pregnant, 2 going to full term. The writer thinks that the danger of rupture of the uterus in these cases is purely theoretical. In 5 cases the operation was imperfect, fibroids being left; however, sarcomatous degeneration of such growths is extremely rare.

He prefers the abdominal operation, and removes the entire capsule of the tumor, resecting part of the uterine wall. Comparing the results of his conservative work with those of supravaginal amputation, the writer considers the former preferable.

**Cystadenoma of the Uterus.**—BANEREISEN (*Beiträge zur Geb. u. Gyn.*, Band ix., Heft 1) removed a uterus in the anterior wall of which was a pedunculated tumor. The pedicle was hollow and communicated with the uterine cavity and the interior of the growth. Anatomically the latter consisted of typical lymphadenoid tissue. The glandular structures were continuous with the glands of the uterine mucosa.

**Recurrence after Extirpation of the Cancerous Uterus.**—MACKENRODT (*Monatsschrift f. Geb. u. Gyn.*, Band xix., Heft 6) asserts, as the result of his observations in 80 cases, in 95 per cent. only the intrapelvic lymph nodes were affected. Since in at least one-half of all cases of cancer of the uterus, even in the early stage, the glands are diseased, failure to remove them means that recurrence is inevitable. The writer adds that in at least three-fourths of the so-called inoperable cases the deeper nodes are affected late in the course of the disease, so that a radical operation may be possible if not delayed too long.

**Cysts of the Mesentery.**—HAAS (*Zentralblatt f. Gynäkologie*, 1904, No. 50), in reporting a case, states that the principal diagnostic points are sudden acute pain in the abdomen, associated with the presence of a tense, elastic tumor, with slight mobility and tender on pressure. The tumor has no apparent connection with the pelvic or abdominal viscera except the intestines. A coil of gut can usually be demonstrated to be adherent to the tumor, which moves with it.

Enucleation of the cyst is the best method of treatment, provided that this can be done without too great loss of blood. If a radical operation is impracticable the sac may be stitched in the wound and drained.

**Inoperable Cancer of the Uterus.**—LICK (*Monatsschrift f. Geb. u. Gyn.*, Band xx., Heft 1 and 2) reports 70 cases treated by curettement, cauterization and subsequent applications of perchloride of iron, with one death following operation.

Hemorrhage and sloughing were eliminated in nearly every instance; 70 per cent. of the patients died during the first year, 9 women lived from one to one and one-half years, 1 survived for two years, and 1 over four years. The average duration of life after operation was 228 days.

**Injury to the Rectum during Gynecological Examinations.**—KELLY (*Weiner klin. Therapeut. Wochenschrift*, 1904, No. 29) reports 4 cases in which injuries occurred. The cause was probably diminished muscular resistance of the rectal wall due to advanced age.

The treatment advised is laparotomy and suture of the rent, unless the perforation can be reached and repaired by vaginal section. A rectal tube should be introduced and the bowels constipated for five or six days.

In elderly subjects rectal palpation must be practised with care, without keeping the finger too stiff.

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**Operative Treatment of Climacteric Hemorrhages.**—QUEISNER (*Zentralblatt f. Gynäkologie*, 1904, No. 51) describes his method of treating obstinate cases in which ordinary methods fail and hysterectomy is refused. A T-shaped incision is made in the anterior vaginal wall, the bladder is dissected from the uterus, and the vesicouterine pouch is opened. The raw surface on the bladder is covered by the anterior peritoneal flap. The uterus is drawn downward, split in the median line, and both halves are sutured to the edges of the vaginal wound. The uterine mucosa, being then thoroughly exposed, is cauterized with the Paquelin. The after-treatment consists in vaginal douches, the patient being allowed to leave her bed on the fourth day. Two successful cases are reported.

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**Results of Alexander's Operation.**—REIFFERSCHIED (*Archiv f. Gynäkologie*, Band lxxiii., Heft 1) reports 241 cases from the Bonn clinic; 96 were kept under observation, 8 of which were failures. In 18 cases one or both ligaments were either not found or were torn in pulling out. Better results were obtained when the canal was not opened.

Stress is laid on the importance of frequent emptying of the bladder during the first few days after operation.

From experiments on the cadaver, the writer is led to take an opposite position from Doléris and others, who claim that the round ligament can always be found at the external ring, even in infants and in the aged.

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**Entrance of Fluids into the Tubes.**—THORN (*Zentralblatt für Gynäkologie*, 1894, No. 38), from a series of experiments with the cadaver, as well as clinical observations, arrives at conclusions contrary from Döderlein, who affirmed that fluids injected into the uterine cavity frequently enter the tubes and even escape into the peritoneal cavity. In all the reported fatal cases the writer thinks that there was a strong probability that the uterine wall was perforated. The greatest danger, he believes, in injecting caustics is from necrosis of the wall and entrance of the fluid into the veins, especially after curettement for malignant disease of the endometrium. Hence Braun's syringe is not such a dangerous instrument as has been represented, provided that only a few drops are injected at a time, the chances being a thousand to one that superfluous fluid will escape from the os rather than enter a normal tube.

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**Injuries to the Genital Tract during Coitus.**—SAKS (*Zentralblatt für Gynäkologie*, 1904, No. 38) reports the following cases:

Cases I. and II. Two newly married women had profuse hemorrhage for an entire day following the first coitus from an artery in the ruptured hymen, which was controlled in one case by pressure with

tampons saturated in a 20 per cent. solution of ferripyrrin, in the other by a solution of perchloride of iron.

Case III. A multipara, aged twenty-five years, had intercourse in a semiprone position. She was seized with a severe pain in the abdomen followed by profuse bleeding. Examination showed a tear in the right vaginal fornix. The hemorrhage was controlled by a tampon and the patient was removed to the hospital, where it was necessary to give a subcutaneous injection of saline solution. She made a good recovery.

Case IV. A girl, aged twenty-five years, bled for three days after her first coitus so that she fainted in the street and was brought to the hospital. A tear was found in the rectovaginal septum, the hymen being intact. The wound healed in a few days after removal of a tampon which had been placed in the vagina.

Case V. Repeated coitus in a newly married woman was followed by sharp hemorrhage, which was due to a lacerated hymen, and was checked by a solution of the perchloride.

Commenting on these cases, the writer calls attention to the comparative infrequency of these lesions, less than 200 having been recorded. Twenty-two fatal cases have been reported from hemorrhage or infection. In one instance a man lost three wives in succession from laceration of the posterior vaginal fornix during the first marital approach.

The cause is usually some anomaly of the female genitals, or unusual size of the male member, or the deeper lesions of the vagina may be due to unnatural positions during coitus. The writer disagrees with those observers who attribute them to excessive sexual excitement on the part of the female.

## DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF

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OF PHILADELPHIA.

**Purulent Maxillary Sinusitis.**—DR. LIAMBEY (*Annales des maladies de l'oreille, du larynx*, etc., December, 1904) reports a case of maxillary sinusitis in a girl aged seventeen years, with a fistula at the inferior angle of the left orbit, consecutive to an odontoma. The affection was said to be of seven years' duration. The middle meatus contained mucous polypi bathed in pus. Puncture of the inferior meatus and syringing through the cannula discharged fetid pus, both by the nose and by the fistula. The upper left canine tooth was absent, and there was a fistula there from which pus exuded on compression of the gums. The sinus was opened and found full of pus and fungosities. As the breach in the opening was being enlarged, an odontoma was forced out, evidently corresponding to the absent canine tooth. The sinus was faith-

fully curetted, and the patient gradually recovered in a little less than six weeks. This case has been recorded on account of its rarity, the reporter having no knowledge of an analogous case in medical literature.

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**Sarcoma of the Tonsil Apparently Cured by Exposure to Roentgen Rays.**—DR. CHARLES LESTER LEONARD (*American Medicine*, December 3, 1904) reports, among other cases, one of sarcoma of the tonsil apparently cured after a series of treatments, external and internal, twice a week, with a high vacuum, and without injury to either skin or mucous membrane. The patient has since been actively engaged in his insurance business for fourteen months.

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**Primary Tuberculosis of the Pharyngeal Tonsil.**—That the lymphoid tissue at the vault of the pharynx may become the seat of tubercle as well as the tonsil and other lymphoid tissue elsewhere in the throat is well known, but primary tuberculosis is very rare and difficult of substantiation. In the *Medical Record*, October 8, 1904, DR. DONALD M. BARSTOW refers to a case of "Supposed Primary Tuberculosis of the Pharyngeal Tonsil" in a man, aged twenty-nine years, who had suffered with cough for some two years, and for three or four months with a continuous cold in the head and copious expectoration. Examination of the sputum revealed "innumerable tubercle bacilli and quite a large number of streptococci." Posterior rhinoscopy revealed a large amount of very soft and friable adenoid tissue in the vault of the pharynx. Under cocaine this was removed with little difficulty. Two weeks later examination of the sputum "required long-continued search to find tubercle bacilli, and when found they were either isolated or in small groups;" hence the inference that this might be a case of primary tuberculosis of the pharyngeal tonsil. The patient gained in weight rapidly, and was soon dismissed from supervision.

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**Foreign Body in the Larynx Removed through the Natural Passages.**—The case is reported by DR. HENRY COUSSIEU (*Annales des maladies de l'oreille, du larynx*, etc., March, 1904). A nervous lady, an hysterical subject, insisted that she had swallowed a pork bone while taking soup, and that she could feel it in her neck. It could not be detected upon laryngoscopic examination, and there were no physical signs to denote its presence in the air passages. Nearly a month later, on presenting herself with a story of bronchitis, a putrid odor from the mouth and a continuance of the sensation of the bone in her neck, laryngoscopic inspection revealed the bone, sure enough, impacted below the vocal bands, beneath which a thin edge of a flat foreign body could be seen in the middle vertical line. This was readily removed with forceps, and measured 29 mm. in its greatest length and 18 mm. in its greatest width. The case is illustrated with wood-cuts, showing the laryngoscopic image and the manner of extraction.

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**Live Foreign Bodies in the Larynx.**—In an excellent, researchful, though rather prolix article on the course to take in cases of animated foreign bodies in the human larynx (*Revue de hebdomadaire de laryngologie, otologie, et rhinologie*, March 12, 1904), DR. LINARAS reviews almost the entire literature of the subject, and mentions, among other personal observations

of cases of leeches in the air passages, two which may be noted here for their singularity. In one the leech was situated at the anterior commissure of the vocal bands subglottically. An appointment was made for the patient to go to a hospital for operation; but in the interim an Arabian acquaintance whom he consulted advised him to gargle with a decoction of fresh tobacco-leaves. This he did, and shortly afterward coughed out the leech without any trouble.

In the other case the leech was found to have left the larynx and to have attached itself to the vault of the pharynx. It eluded the first attempt to catch it with forceps by sliding down the pharynx, but eventually crawled up again, when it was caught and extracted.

**Morbid Growth of the Larynx of Traumatic Origin.**—DR. JOHN EDWIN RHODES (*Chicago Medical Recorder*, June, 1904) reports a case of a lad whose neck had been caught between a plank and the rollers of a machine. He spat blood for six hours and became dyspnoëic and dysphonic. He gradually improved and left the hospital in three weeks, with subsidence of the acuter symptoms, but with continuance of the hoarseness and difficulty in breathing. Nearly two months later he returned with a small abscess in the median line over the thyroid cartilage, which, on opening, revealed the presence of a grape-seed, which had probably made its way there from the œsophagus.

Laryngoscopic exploration revealed marked thickening of the ventricular bands and of the arytenoids, with such deformity of structure as to reduce the calibre of the larynx to scarcely one-fourth of its normal size. From the right ventricular band there projected a mass of tissue the size of a small bean, which acted as a valve in closing the lumen of the larynx during both inspiration and expiration. Attempted removal with crushing forceps having failed, a preliminary tracheotomy was performed a few days later, and, after cocainization of the larynx, the growth was removed with a cold-wire snare without difficulty. At the time of the report the patient's breathing was easy and the voice fairly good, although the lumen of the larynx remained much diminished by the distortion which had followed the accident.

**Double Abductor Paralysis of Traumatic Origin.**—DR. LAMBERT LACK recently exhibited to the Laryngological Society of London (*Journal of Laryngology, Rhinology, and Otology*, June, 1904) a man who had had complete bilateral paralysis for eighteen months as a result of a throat-cut almost completely dividing the trachea at its junction with the larynx. It was supposed that both recurrent nerves were injured. The patient was wearing a T-shaped tracheotomy tube, as there was a narrowing of the calibre of the windpipe just above the external opening into the trachea large enough to admit the tip of the little finger. The paralysis was complete on the left side, with a slight movement on the right side.

Sir Felix Semon thought it must have been a very extensive cut to have reached both recurrent laryngeal nerves, and that it was not easy to understand why the other neighboring structures should have escaped. In his opinion probably the most plausible explanation was that there had been a good deal of new formation of cicatricial connective tissue in the neighborhood of the recurrent laryngeal nerves which had gradually compressed them.

<sup>5</sup> **Hemorrhage after Tonsillotomy.**—DR. OSCAR WILKINSON (*Journal of Eye, Ear, and Throat Diseases*, July–August, 1904) reports a case of hemorrhage after tonsillotomy relieved by the use of adrenalin. After a double tonsillotomy under nitrous oxide on a girl, aged seventeen years, there was free hemorrhage, which was controlled by the application of adrenalin solution 1 : 1000 and ice gargles. Profuse hemorrhage recurred in two hours. Applications of adrenalin solution controlled the hemorrhage but for a short time. Ten drops of the solution were then given internally, followed by a similar dose in twenty minutes, after which there was no more bleeding.

**Prevention of Postoperative Hemorrhage in Intranasal Surgery.**—In a paper on "The Collodium Dressing for Intranasal Surgery," presented by DR. CHARLES W. RICHARDSON, at the Ninth Annual Meeting of the American Academy of Ophthalmology and Otolaryngology, held at Denver, August, 1904 (*The Laryngoscope*, September, 1904), attention is called to an article by DR. KASPER PISCHAL, of San Francisco, on "Collodium after Nose Operation," published in the *Archives of Otolaryngology*, vol. xxxi., 1902, and which has received but scant notice from the profession. Dr. Richardson has modified Dr. Pischal's method, and finds that if collodium is properly applied to the whole wounded surface it will absolutely control postoperative bleeding.

**Fatalities in Operations upon the Nose and Throat.**—At the annual meeting of the American Laryngological Association, held at Atlantic City, in June, 1904, DR. FRANCIS R. PACKARD presented a study of the fatal results of operations upon the nose and throat (*The Laryngoscope*, September, 1904), including and supplementing tables compiled by DR. HOLLOWAY in 1896 and DR. F. W. HINKLE in 1898. Three tables have been prepared, showing 26 deaths attributable to a general anæsthetic, 22 deaths resulting from operations in which the fatal issue was not the result of the anæsthetic, and 5 deaths following operations in which the exact cause of the fatal issue was not given. The total number of deaths attributable to a general anæsthetic was 26: 24 from chloroform, 1 from chloroform and A. C. E. mixture, and 1 from ether. There were 14 deaths from hemorrhage following the removal of tonsils or adenoids, 11 in males, 2 in females; and the sex of 1 case was unmentioned. One death from sepsis and exhaustion is reported following tonsillotomy in a boy. Of the remaining 7 deaths by meningitis, 2 followed an attempt at the correction of a septal deformity; 1 followed an application of perchloride of iron for epistaxis; 1 followed an operation by external access for removal of nasal polypi and orbital tumor (death from purulent leptomeningitis); 1 followed cauterization of middle turbinal with the electric cautery; 1 followed probing the frontal sinus and injection of the lacrymal canal, and 1 followed removal of exostosis.

Of the 5 cases in which Dr. Packard was unable to ascertain the exact cause of death, 1 death was attributable to each of the following operative procedures:

Curettement of nasal polypi.

Galvanocauterization of the middle turbinates, followed by hemorrhage requiring tampon. Death in three days.

Galvanocauterization for bony and membranous occlusion of the right nasal fossa. Death in six days after operation.

Curettement for chronic purulent rhinitis. Death in three days.

Removal of polypi with snare. Empyema of antrum of Highmore. Death eleven days after operation.

In each of these instances death occurred a number of days after the operation, and the history of the cases leads to the inference that it was due to meningitis.

The author of the paper concludes that from the above it is readily inferred that meningitis is a complication of intranasal operation and should not be lightly regarded. It has occurred and proved fatal in enough instances to make us realize that the close relationship existing between intranasal structures and the meninges is not to be overlooked in our intranasal operative work.

## OTOLOGY.

UNDER THE CHARGE OF

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**Three Cases of Labyrinth Trephining.**—BOTEY states that the surgery of the internal ear is still in its early stages, and that excision of that part of the labyrinth accessible through a large opening into the middle ear has but recently been definitely done with success, warrants a more exhaustive notice of the author's paper than would ordinarily be accorded within the limits of a review, but it will still be necessary to refer the reader to the original for the technique of the several operations, the very careful and minute observations made, and the complete reports of the cases.

In all of the operations the primary postaural openings were made sufficiently large to afford free access to and inspection of the inner tympanic and antral walls, and the operation upon the petrous portion of the temporal bone was done by means of the gouge and curette, supplemented by small electric burrs.

The first case was that of a man, aged twenty-six years, who had suffered from a suppurative process in the left middle ear for twenty years, with recently resultant severe occipital pain, excessive tinnitus, and violent attacks of vertigo; there was caries of the epitympanum and antrum, accompanied by labyrinth suppuration, and the operation, which included an extensive incision of the mastoid and middle ear and opening of the external semicircular canal and first whorl of the cochlea, resulted in recovery.

The second case was that of a boy, aged fourteen years, who, following scarlet fever in his second year, had persistent suppurative discharge from the left ear, with occasional exacerbations and symptoms



of pus retention; latterly there had been attacks of vertigo and vomiting; there was destruction of the pars flaccida, cholesteatomatous accumulation in the epitympanum, and antrum and labyrinth suppuration.

The operation consisted of a mastoid exenteration with a large opening into the external semicircular canal and cochlea, the latter being effected by removal of the inner tympanic wall within a line drawn from the posterior end of the oval window to the posterior end of the round window; then, in a curve forward and downward from the anterior edge of the oval window, and then posteriorly in a curve downward to within two millimetres of the tympanic floor and upward to the round window, the opening into the semicircular canal being made with burrs. In this case also a cure was effected.

The third case was that of a man, aged thirty-five years, having a history of bilateral middle-ear suppuration since infancy, with occasional congestive exacerbations in the left ear, accompanied by deep-seated pain extending into the neck and head, but unaccompanied by tinnitus, vertigo, or vomiting. In spite of feebleness his gait was normal, and the tests of von Stein indicated no change in the static and dynamic function of the labyrinth. There was absolute loss of hearing in the left ear, slight dysphagia, and paræsthesia of the left side of the palate with paralysis of the left vocal cord, probably due to lesion of the vagus at the point of its exit.

In addition to the chronic bilateral middle-ear suppuration and necrosis of the left labyrinth, there was a cerebral and cerebellar abscess.

There were two operations: the first a tympanomastoid exenteration with opening of the middle cerebral fossa, and the second, an opening of the posterior cerebral fossa with extraction of the petrous portion of the temporal bone to the depth of the internal auditory canal, and death from shock.

The existence of large openings into the labyrinth, as evidenced in the examination of these three cases, is demonstration of the ease with which pus may enter that cavity in persistent suppuration of the middle ear, especially where there is cholesteatomatous blocking of the epitympanum and antrum, and the cases are also evidence of the fact that operation upon the labyrinth, by way of the epitympanum and antrum, with large opening of the antrum and mastoid, is easily possible.

The fact of the breaking of two burrs inside the external semicircular canal, in the second case, is a demonstration of the extraordinary hardness of the labyrinthine capsule in cases of otorrhœa with osteosclerosis, and at the same time suggests the necessity of using burrs with relatively large shanks.

In the opinion of the author the existence of granulations emerging from a fistulous tract, or from one of the windows, confirms the diagnosis of labyrinth suppuration, especially when the otorrhœa is accompanied by violent attacks of vertigo, vomiting, and disturbances of equilibrium.

Tinnitus, as a rule, does not occur in suppuration of the labyrinth; it is often wanting; when it appears it lasts but a short time, and it occurs only at the beginning of the pyolabyrinthitis:

When a patient in the course of a chronic otitis media is suddenly attacked with vomiting and dizziness, with great inco-ordination of movement, notwithstanding their violence and tenacity, it is not neces-

sary to infer always that pus has penetrated the semicircular canal or the vestibule. It may happen that pyolabyrinthitis does not exist, and that the labyrinthine symptoms are due to simple peripheral compression of the neuroepithelial terminations of the auditory nerve in the ampullæ and the membranous vestibule, occasioned by the presence of cholesteatomatous masses lodged in the attic and aditus, which, by their volume and eccentric growth, push from without inward upon the perilymph and endolymph. Vertigo also may be due to congestion extending from the middle to the inner ear without the entrance of pus or pyogenic germs.

The author cites cases of otorrhœa with dizziness and violent vomitings of long duration, which, despite these symptoms, had no pus in the labyrinth, and in one operative case he found caries and necrosis of the inner wall of the middle ear with absolute integrity of the labyrinthine membrane. In two of these cases, after radical operation with slight curetting of the granulations and removal of small sequestræ, the patients recovered, the tuning-fork and the tests of von Stein showing that the acoustic nerve, on the side operated, effected perfect co-ordination of voluntary movements.

The third case demonstrates clearly that a pyolabyrinthitis may exist without tinnitus, vertigo, and other disturbances of equilibrium, which reduces the diagnosis to the category of simple surmises, except for the perceived symptoms of suppuration of the labyrinth. This case also shows the possibility of Chaput's operation (resection of the petrous bone), especially when the petrous bone is necrosed, without reference to the existence of the internal carotid artery at the superior part, the sequestræ usually being easily mobilized.

In practice it is rarely necessary to remove so great a part of the petrous bone, Chaput never having done so complete an operation on the living subject.

It is nearly impossible to avoid facial paralysis in resecting the petrous bone, as it is necessary to cut the facial nerve to remove the labyrinth.

The conclusions to be drawn from these three cases and from the author's experience in cases presenting labyrinthine symptoms with suppuration of the middle ear, are given by him as follows:

1. In pyolabyrinthitis cochlear disturbances of the acoustic nerve, such as tinnitus and subjective noises, are very inconstant, quite early, and always temporary. The noises are possibly due to the inflammatory participation of the organ of Corti, the peripheral neurons being more easily destroyed by suppuration than the neuroepithelial terminations of the auditory nerve in the vestibule and in the semicircular canals.

2. Taking into account the small volume of the membranous labyrinth, suppuration nearly always extends over the entire surface, by rapid diffusion of pus, to the whole cochlea, and deafness is complete. This statement the author maintains on his experience with these three cases, and in spite of the contrary opinion of Jansen and Hinsberg, who believe that suppuration frequently affects a part of the labyrinth, principally the external semicircular canal.

3. The most minute examination of the ear, and at the same time the study of the progress of the disease and the appearance of the most characteristic disturbances of equilibrium, do not indicate, in advance, with certainty, the existence of pus in the labyrinth. Only during operation can it be ascertained whether a pyolabyrinthitis really exists

or whether the lesion of the inner wall of the middle ear communicates with the labyrinth.

4. The communications of the middle ear with the internal ear in suppuration are nearly always very small; they can consequently easily be passed unperceived if they are not carefully sought for with a probe.

5. Opening the whole labyrinth with extraction of the promontory, from the oval window to the round window, to the floor of the middle ear, and to the neighborhood of the Eustachian tube, according to the technique advised, ought, in the author's opinion, to be carried out on all occasions, even in cases where the pus is only found in the interior of the external semicircular canal. Not only is the drainage easier, but the pus cannot spread to the inner nooks of the labyrinth.

6. In doubtful cases where some auditory perception remains in the diseased ear, it is better to do a tympanomastoid exenteration and wait for four or five days. If, at the termination of this time, labyrinthine disturbances persist with the same intensity, it is permissible to open the labyrinth by means of a second operation, for an infection is sure to be found.

7. Nystagmus, which is often observed in accidental lesions of the horizontal semicircular canal and in all cases of subacute irritation of the labyrinth, is a symptom rarely observed in practical otology on account of its being slightly noticeable and of short duration.

8. A large opening of the labyrinth, correctly done, with the revolving burr, is less liable to produce dangerous shaking and the breaking up of adhesions which keep the pus in a limited tract of the inner ear and do not allow it to extend, by way of the aqueducts, into the cranial cavity, this operation is one of little danger, and the mortality need not be expected to be above 4 per cent.

9. All labyrinthine fistulæ, which are only findings of evidence, without vertiginous symptoms, without tinnitus or deafness, should not be disregarded, as advised by Jansen and Hinsberg. It is advisable to open the fistula into the labyrinth immediately, the external opening of the fistulous tract being opened carefully without interference with the membranous labyrinth, removing the superficial granulations if they exist, to observe if the pus is deeply situated, and then awaiting the results of operation. If at the end of three or four months, when the operated cavity has epidermatized, the passage of communication between the middle and internal ear continues to discharge pus, and especially if vertigo and disturbances of equilibrium coexist, it is necessary to make a large opening into the labyrinth. If the fistulous tract no longer exists after epidermatization of the operative cavity the cure may be considered complete.

10. Pus can be present in the labyrinth without disturbances of equilibrium, the tests of von Stein being negative. In the unique case cited operation demonstrated pyolabyrinthitis. The whole labyrinth was destroyed, and in consequence there was complete deafness on the affected side.

11. It is necessary that the membranous labyrinth be not destroyed in order to have labyrinthine symptoms, so that the tests of von Stein will indicate the disorders of equilibrium. Where it is destroyed the well labyrinth will in time make up for the static functions which have been abolished, and the patient no longer exhibits labyrinthine symptoms.

12. The vagospinal can be wounded at its exit from the skull either

by a particle of bone (the vaginal process of the petrous bone) or by an instrument. In such a case there would be paralysis of the palate and of the vocal cord of the corresponding side, as happened in the third case cited. This tends to prove that the facial nerve has nothing to do with the innervation of the soft palate.

**The Significance of Swelling of the Cervical Lymph Glands in Middle-ear Suppurations.**—STENGER (*Archiv f. Ohrenheilkunde*, Band lxii. pp. 3 to 4) considers the presence of swollen lymph glands in the region of the ear and in the region of the sternocleidomastoid of great practical significance as an aid in determining the necessity of operative interference in cases of middle-ear suppuration. According to Poirier, the glands of importance in this connection are: (1) The mastoid lymph glands, ordinarily two in number, found in children connected by two or three lymph vessels over the place of origin of the sternocleidomastoid. They receive their afferent vessels from the tympanum and the posterior wall of the external auditory canal. Their efferent vessels lead into the upper group of lymph glands beneath the sternocleidomastoid. (2) The upper group of glands beneath the sternocleidomastoid, which extend from the tip of the mastoid process and the posterior belly of the digastric to the point where the omohyoid crosses the great neck vessels. An outer and inner portion of these glands can be distinguished.

In chronic middle-ear suppurations the swelling of any of these glands may be expected. In acute suppuration swelling of these glands is not the rule; but when the mastoid also is affected, one finds, as a rule, painfully swollen glands beneath the mastoid and behind the sternocleidomastoid. This glandular swelling is of especial diagnostic value in cases of acute middle-ear suppuration which run their course without especial symptoms, and in which the long-continued suppuration is the only fact pointing to an involvement of the mastoid cells. The author points out that the glandular swelling in this region may be due to other causes—*e. g.*, diseases of the scalp and tonsillar affections; and that this must always be borne in mind.

## DERMATOLOGY.

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**The Pathology of the Tuberculides in Childhood.**—NOBL (*Dermatologische Zeitschrift*, Band xi., Heft 12), among 430 children suffering from various diseases, has seen the papulonecrotic tuberculide thirteen times, and accordingly believes this form of lesion is a by no means infrequent one. The eruption is composed of small nodules, pustulo-

ulcerative and necrotic, usually discrete, but sometimes grouped, having a preference for the extensor surfaces of the extremities, the lumbar region and the buttocks; it corresponds completely with the affection described by Barthelémy under the name *folliculis*. All the children in whom this form of eruption was observed without exception presented other evidences of scrofulotuberculosis, most commonly alterations in the lymphatic glands. In 11 of the 13 cases observed scrofulous gummata and lichen scrofulosorum accompanied the papuloulcerative lesions. Although it was not possible to demonstrate the presence of tubercle bacilli in a single case, their structure resembled that of actual tubercle. Tuberculin injections were regularly followed by elevation of temperature. The local phenomena either affected all the forms of eruption present, or were confined to types of lesion other than the necrotic nodules, so that no very definite conclusions could be drawn from the results.

The author believes that this form of eruption is due to organisms whose vitality has been so greatly weakened that when they arrive in the skin they die after giving rise to formative irritation. So small a quantity of toxins is produced by these weakened organisms that little or no reaction follows injections of tuberculin.

**Acne Telangiectodes.**—PICK (*Archiv f. Dermatologie und Syphilis*, Band lxxii., Heft 2) reports two cases of the affection which was first described by Kaposi under the name *acne telangiectodes*. Distributed over the scalp, face, upper portion of the chest, on the forearms, hands, and legs were numerous small nodules, part of which in the course of the disease underwent suppuration, part were absorbed. These lesions were most abundant in the face, and upon disappearing left depressed scars like those following *acne varioliformis*. Through the constant appearance of new lesions the course of the disease was an eminently chronic one, extending over many months. Histologically the lesions were composed of a granulation tissue containing numerous epithelioid and giant cells. Although many of the elements characteristic of tuberculous tissue were present, yet it was not difficult to distinguish it from such tissue. Although many sections were examined for tubercle bacilli none were found. The author's conclusions are as follows: *Acne telangiectodes* is an affection *sui generis*, and not identical with *lupus follicularis disseminatus*; but it is identical with the *acnitis* of Barthelémy, and must be distinguished from the disease known as *folliculis*. It presents no sort of etiological relationship to tuberculosis, and should be separated from the tuberculomata and the tuberculides. It does not take its origin in the sebaceous glands and, therefore, does not belong to *acne*. The marked implication of the sweat glands in the inflammatory changes may possibly have some etiological significance.

**The Cutaneous Manifestations of Leukæmia and Pseudoleukæmia.**—NICOLAU (*Annales de dermatologie et de syphiligraphie*, Nos. 8 and 9, 1904), in a paper of some length, reports the results of a clinical and histological study of two cases of cutaneous leukæmia. The first of these cases was a man with a lymphatic leukæmia pursuing a relatively slow course. In the face, upon the scalp, and in the temporal region were foci of nodules having a marked tendency to ulceration which were

subsequently transformed into soft, infiltrated, nodular plaques, more or less elevated above the surface, persisting indefinitely. There was likewise a diffuse infiltration of the lobule of the left ear, which, increasing, became a pedunculated tumor with no tendency to ulceration. Microscopic examination of the tumor of the ear revealed a structure composed exclusively of round cells having all the characters of lymphocytes lodged in a fine connective-tissue reticulum—that is, a true lymphoma. The author regards the cells of leukæmic tumors as true lymphocytes, having their origin in the blood.

The second case was one of generalized exfoliative erythrodermia with fine, dry scales, accompanied by moderate pruritus, occurring in a man, aged sixty years, presenting hypertrophy of the ganglia and spleen, with a relative increase in the percentage of the lymphocytes in the blood.

The autopsy and histological examination fully confirmed the clinical diagnosis of pseudoleukæmia. From the study of his own case and of similar ones reported by other observers Nicolau is of the opinion that the exfoliative dermatitis is not an accidental occurrence, but is directly dependent upon the pseudoleukæmia. He also discusses the relationship of this dermatitis to the pityriasis rubra of Hebra which it resembles clinically, and concludes that this latter disease is composed of three groups, one of which is closely related to tuberculosis, the second is intimately associated with pseudoleukæmia, while the third is related to none of the foregoing and should be considered as true idiopathic pityriasis rubra.

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**Joint Affections in Psoriasis.**—MENZEN (*Archiv f. Dermatologie und Syphilis*, Band lxx., Heft 2), who has studied the records of the dermatological clinic at Bonn with a view of learning what relationship, if any, exists between affections of the joints and psoriasis, found that in only 5 out of 1000 cases of the latter disease observed during a period of twenty-three years was there any accompanying disease of the joints; 3 of these cases were studied most carefully, and in none was it possible to demonstrate any probable relationship between the disease of the joints and the eruption.

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**An Almost Complete Cure of Tuberculous Lupus by Permanganate of Potash.**—HALLOPEAU and NORERO (*Annales de dermatologie et de syphiligraphie*, November, 1904), at a *séance* of the Société Française de Dermatologie et de Syphiligraphie, reported a case of extensive lupus which had been almost entirely cured by applications of solutions of permanganate of potash. The patient was a girl, aged fourteen years, who, since she was five years old, had had an ulcerating lupus of the face, which upon her entrance into the hospital occupied the lower two-thirds of the nose, the cheeks, and the anterior portion of the neck. The diseased areas were treated by the application of compresses wet with a solution of permanganate of potash, generally 1:50, sometimes 1:20. Under the influence of this medication the ulcerations gradually cicatrized. At the same time an extensive ulcerating lupus of the left leg was cicatrized by the same medication.

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**The Treatment of Port Wine Nævus by Radium Bromide.**—HARTIGAN (*British Journal of Dermatology*, December, 1904) exhibited a case of

port wine nævus at a meeting of the Dermatological Society of London, in which treatment with radium bromide had been productive of decidedly encouraging results. The patient was a woman, aged twenty-six years, with a nævus covering the left cheek and the side of the nose. The two specimens of radium employed weighed 10 mgm. each, and were of the highest known radioactivity. Thirty-nine exposures, varying in duration from a half to one hour, were made at intervals of a week. At the time the patient was exhibited the nævus had entirely disappeared with the exception of a few small areas which had not yet been treated.

[The members of the Society before whom the case was presented expressed the opinion that the result of treatment was "distinctly encouraging." A photograph accompanies the report of the case, and if this picture shows the nævus at the close of the treatment, when the reporter states the mark had "entirely disappeared with the exception of a few small untreated areas," the result does not seem to the observer of the picture to be entirely satisfactory, as the photograph shows either part of the nævus remaining or scarring. If it be scarring, any treatment that will cause scarring in the treatment of nævi is to be deprecated.]

**Thigenol.**—SAALFELD (*Jour. mal. cut. et de syph.*, November, 1904) experimented with this new substance, put forward as a succedaneum to ichthyol. It is a composition of iodine and ichthyol, in which occurs 10 per cent. of sulphur in an organic state of combination. Thigenol possesses a dark-brown color and a syrupy consistence; is inodorous, almost insipid; soluble in water, alcohol, and glycerin. Applied to the skin it dries rapidly, and it does not stain the linen. It is a vaso-constrictor, is useful in inflammations, is drying, and favors resorption. It calms itching, as shown in 124 observations in eczema. In seborrhœic inflammations in solution it was found especially useful. It is a mild remedy, and in the author's experience was of no value in psoriasis. In phlebitis, bandaging with thigenol, glycerin, and water, equal parts, gave very good results.

**Treatment of Impetigo.**—HONCAMP, of Berlin (*Monatshefte f. prak. Derm.*, Band xxxix., No. 12), gives a clinical note on the value of bismuth chinolin rhodonate (Oudim Edinger), which is applied as a powder after removal of crusts, with a wooden spatula, as metal instruments are to be avoided on account of ready oxidation. At the moment of application a slight burning is experienced, which soon passes away. This can be avoided by mixing the drug with equal parts of starch. Following the application, yellow, loose crusts form which become brownish. A bandage or covering is not required. The impetigo lesions heal under the crusts in three or four days.

**Clinical Results Concerning Atoxyl.**—BIRINGER (*Jour. mal. cut. et de Syph.*, November, 1904, p. 848) experimented with this new drug at the clinic for cutaneous diseases at Bonn. The drug is a white, crystalline, inodorous, almost insipid powder, soluble in 20 per cent. of hot water. The solution takes on a yellowish tint on cooling, and bases to take up about 2 per cent. of atoxyl dissolved. The toxicity is about forty times less strong than that of the other inorganic arsenical preparations. Forty-two patients received subcutaneous injections of 20 per cent.

atoxyl, either in the cellular subcutaneous tissue of the interscapular region or in the muscular tissue of the thigh, the latter region being preferable. Infiltrations very rarely followed at the point of injections, and the pains were very slight. The average dose was a Pravaz syringe-ful every other day. In lichen rubra the treatment was exclusively by this method, the itching decreasing after seven or eight injections, on the average twenty-five or thirty being necessary for the cure. One of the patients had never tolerated arsenical treatment, but this was well borne. One case of flat wart was cured very rapidly; and one case of dermatitis herpetiformis was cured after twenty-four injections. The drug is very easy to manage and can be made of great service in cutaneous diseases.

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**Atrophy of the Entire Skin of Face Caused by Roentgen Rays.**—DR. NOBL (*Proceedings of Wiener Derm. Soc.*, February 10, 1904) reports the case of a man, aged thirty years, who was treated with rays for a chronic sycosis, fifty sittings, at a day's interval, five to ten minutes each, at 20 centimetres' distance, having been given. During all this long period there occurred no active reaction. The atrophic lesions developed late, and for two years subsequently had undergone no further change. The skin everywhere was thinned and had a vitreous look, with slight scaling and very fine fissures, the lines being similar to those of old age. The epidermis was rough, like tissue paper, beneath which the skin was red, showing vascular ectasias and numerous relics of the sycosis.

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## PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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**The Bactericidal Activity of the Organism under Normal Conditions and during Infections, and Organism of the Body which Protect against Infection.**—HOKE (*Zeitschrift f. Heilkunde*, 1904, Band xxv. p. 197) has investigated the action which extracts of various organs of the rabbit have upon the bactericidal action of normal rabbit serum. He finds that many of these extracts are capable of arresting the bactericidal power of rabbits' serum for anthrax, colon, and typhoid bacilli, the spirillum of cholera, and staphylococci. Liver, kidney, and lymph glands show the most marked antibactericidal power, while leukocytes and bone-marrow have little or no effect. The mechanism of this action was found further to be somewhat complicated and differed from the various bacteria used. For anthrax the arrest of bactericidal action is due to the absorption by the organ extracts of the immune body of the serum.



With typhoid and colon bacilli the extracts of all organs are capable of binding the complement of the serum, while lymph glands and kidney absorb the immune body as well as complement. Both the complement and immune body for staphylococci are taken up by all organs.

Further experiments showed that leukocytes and bone-marrow extracts from normal animals had practically no influence on the bactericidal action of the serum, but if one used the leukocytes and bone-marrow from an animal which had been inoculated with typhoid bacilli or one of the other types of bacteria and killed during the infection, these extracts showed a definite bactericidal action toward that particular organism with which the animal was inoculated. The activity of these extracts was independent of the serum. The extracts of other organs from the inoculated animals showed the same power of arresting the bactericidal power of the serum, as was seen with the organs from normal animals. On the other hand, agglutinins were not bound by liver, kidney, or bone-marrow cells. The author concludes that the bone-marrow is one of the most important organs in the body, in the protection of the organism against infection.

**Trypanosomiasis Expedition to the Congo.**—*Memoir XIII. of the Liverpool School of Tropical Medicine* (London, 1904, WILLIAMS and NORGATE) contains seven papers, the result of an expedition sent to the Congo by the Liverpool School of Tropical Medicine to investigate trypanosomiasis. The first two papers are clinical studies of the disease, and consist of the first and second progress reports of DUTTON, TODD, and CHRISTY. Large numbers of cases were studied, blood examinations of several hundred patients, and many experimental inoculations were done. The organism was found to be always the same as that discovered in 1901 by Dutton in Gambia. Out of 1172 patients whose blood was examined, 103 showed the organism, of which number but 57 were previously diagnosed as having the sleeping sickness. The authors divide the cases clinically into three types: (a) cases with no definite symptoms; (b) cases with few symptoms; and (c) fatal cases showing well-marked symptoms, the most notable being fever, lassitude, weakness, and wasting. This latter type is subdivided according to whether they show sleep symptoms or not. Deep or continuous sleep and lethargy, symptoms described as characteristic of sleeping sickness, were not features of the Congo disease as observed by the authors. No definite relation was noted between the temperature and pulse, and the appearance of the parasites in the peripheral circulation. The trypanosomes were repeatedly found in the cerebrospinal fluid, being discovered in 25 of 37 positive cases of sleeping sickness. In 1 case the organism was found in hydrocele fluid.

The clinical aspects of the disease were shown to vary greatly, from the presence of the organism in the blood without symptoms to cases showing much stupor, a very irregular intermittent fever, and great emaciation, followed by death. The duration of the disease the authors have been unable to determine definitely.

The third paper of the series consists of an account by the same authors of the Congo floor maggot, a blood-sucking dipterous larva, found in the Congo Free State, which they encountered during their work upon trypanosomiasis.

CHRISTY's study of the cerebrospinal fluid in sleeping sickness, based

upon 104 lumbar punctures, constitutes the fourth paper. The organism was found in the cerebrospinal fluid in 35 of the 54 positive sleeping sickness cases. It was more often present near the fatal termination of the disease. When present early in the disease, mania and other cerebral symptoms were usually prominent. The trypanosomes may never find their way into the spinal canal, and the commencement of fever or other symptoms is in no way correlated with the entrance of the parasite into the cerebrospinal fluid.

The fifth paper is a preliminary report by THOMAS and LINTON of many animal experiments for comparing the reactions of the trypanosomes of Uganda and Congo Free State sleeping sickness with those of *trypanosoma gambiense* (Dutton). They found no difference in the various strains of organisms, so that the name *gambiense* (Dutton) must be applied to all trypanosomes with which they worked. They were unable to produce any immunity against the infection and found that there was no transmission of immunity to the offspring.

Two cases of trypanosomiasis in Europeans, reported by DUTTON, TODD, and CHRISTY, and supplementary notes upon the tsetse flies, by AUSTEN, in which a revised synopsis of the species of glossina is given, complete the memoir.

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**Studies in Phagocytosis.**—WRIGHT and DOUGLAS (*Lancet*, 1904, vol. ii. p. 1138) first showed that the phagocytic action of leukocytes is dependent upon the action of a substance in the blood plasma, which is necessary to render the bacteria available for phagocytosis. This substance they call "the opsonin."

HEKTOEN and REUDIGER (*Jour. of Infectious Diseases*, 1905, vol. ii. p. 128) have carried the work farther and have studied the action of temperature and of different chemical substances upon these bodies—opsonins—concerned in phagocytosis. They followed Leishman's method of bringing together fluids containing leukocytes and bacterial suspensions, and then counting in stained smears the average number of bacteria taken up by each leukocyte. The experiments of Wright and Douglas were confirmed and were shown to hold for the leukocytes of several species of animals not previously used. The action of the leukocytes of various animals was found to be unequal in their phagocytic powers, and there was a great difference in the amount of the phagocytosis called forth by the various organisms experimented with, the strain of pneumococcus used calling forth practically none. The authors consider that this property may be utilized to separate organisms.

No phagocytosis was observed when leukocytes washed in salt solution were exposed to bacteria that had not been in contact with blood serum, but after bacteria had been digested with normal serum they became "sensitized," and phagocytosis took place even after the bacteria so treated were washed and suspended in normal salt solution. The blood sera from various animals were found to sensitize a non-virulent streptococcus so that it was taken up by human leukocytes. Low temperatures (1° to 4° C.) retarded "sensitization," and the amount of phagocytosis was found to decrease as decreasing amounts of "sensitizing" serum were added.

The experiments of Hektoen and Reudiger show that the serum loses its sensitizing power when heated to between 54° and 60° C. Sensitized streptococci heated to 62° to 63° C. are not taken up by leukocytes

and cannot be resensitized. The authors believe that opsonins, like toxins and complements, possess two groups—haptophore and opsiniferous—which act according to Ehrlich's lateral-chain theory. When various salts and formalin were applied to the mixture of leukocyte-containing fluid and bacterial suspensions, phagocytosis was materially inhibited. This action was further shown to be principally due to the effect of the salts and formalin upon the "sensitizing" serum, while there was no effect produced on the phagocytosis when these chemicals were applied to the leukocytes alone. The authors consider that these chemical substances may neutralize or bind the opsonins so that they cannot act upon bacteria. They think that antiphagocytic action of this nature may be an important factor in the establishment and progress of those infections where phagocytosis is an important factor in the destruction of the organisms.

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**Experimental Typhoid Fever.**—ATLASSOFF (*Annales de l'Institut Pasteur*, 1904, vol. xviii. p. 701) gives an account of his work upon the experimental production of typhoid fever. He first turned his attention to finding some organism which, growing symbiotically with *B. typhosus*, favored the growth of the latter. This was done by growing typhoid bacilli upon acid media with a variety of other organisms. It was found that the typhoid bacilli would grow on a medium containing a higher percentage of hydrochloric acid if cultivated with *torula rosea*, than with any other of a number of organisms experimented with, and that this organism had a decidedly advantageous effect upon the growth of *B. typhosus*. The growth of *T. rosea* did not lessen the acid reaction of the medium.

The experiments were conducted upon very young rabbits, from seven to fifteen days old, when the intestinal tract is nearly free from bacteria, making it less probable for the typhoid bacilli to encounter antagonistic organisms. Four strains of typhoid bacilli, varying in virulence, were used, and were administered by the mouth together with *T. rosea*. In a second series of control experiments typhoid bacilli alone were used.

Sixteen young rabbits were fed with the mixed culture, 15 of which died; 3 were fed with a pure culture of typhoid bacilli, 2 of which died. Of the 15 rabbits that died after a mixed feeding, all showed hyperæmia and punctate ecchymoses of the mucosa of the intestine, and swelling of Peyer's patches. In the cases dying on the seventh or eighth day after feedings, slight ulcerations of Peyer's patches were found. The typhoid bacillus was recovered from the blood in 12 cases, and less frequently from other organs.

The author considers that he has succeeded in producing an experimental typhoid fever much like that seen in infants, where the ulcers are rarely deep. He thinks that the method of feeding gives much better promise for investigation of the disease than subcutaneous or intraperitoneal inoculation. The organism *torula rosea* is frequently found in the human stomach (about 70 per cent.), and may play a definite role in the etiology of typhoid fever.

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**Lesions of the Aorta in Syphilis.**—In Germany the question has been much discussed recently as to whether syphilis produces in the aorta lesions which are typical and characteristic of that disease. A certain

type of arteriosclerosis has been described by many authors as syphilitic, and the main point at issue is the specificity of this sclerosis. CHIARI (*Cent. f. Allg. Path. u. Path. Anat.*, Band xv. p. 137, supplement) at the "VI. Tagung der Deutschen pathologischen Gesellschaft zu Kassel" has considered in detail syphilitic disease of the aorta. As a result of an extensive research he divides arterial sclerosis in general into two types, "A" and "B." The "A" type constitutes the simple atheroma and begins in the intima. It is characterized by a swelling of the tissues, a proliferation of the local cells, fatty degeneration, and, later, regressive alterations leading eventually to the well-recognized endarteritis chronica deformans. The media and adventitia may undergo certain changes which, however, are always secondary to the disease of the intima. The "B" type of sclerosis is quite different. In this group the media and adventitia, instead of the intima, are the primary seats of disease. The surface of the aorta, macroscopically, presents marked irregularities, with corrugations, crevices, clefts, and pittings. The intima is thickened, but there is no calcification; and, further, it is to be distinguished from the "A" type by its localization in the ascending aorta and arch, the abdominal aorta being practically immune. Microscopically the media is found to be the main seat of disease. Through this coat are found small inflammatory areas, formed partly of accumulations of small round cells lying especially about the vessels, which are increased in numbers, partly by granulation tissue or fibrillated connective tissue. Giant cells of the Langhans type may be present or areas of necrosis may form the centre of the inflammatory foci. With the development of connective tissue there is a tendency to shrinkage, and thus are produced the macroscopic scarrings and corrugations over the surface of the aorta. The adventitia likewise presents inflammatory changes combined with a periarteritis and endarteritis proliferans of the vasa vasorum. To this type of affection the author gives the name of "Productive Mesoarteritis." The study of a long series of cases of syphilis and progressive paralysis showed that the productive mesoarteritis was present in more than half of the instances of undoubted syphilis, and in 47 per cent. of the cases of progressive paralysis. The author concludes that syphilis stands in direct causal relationship to this variety of arterial sclerosis, although with our present knowledge of this disease other etiological factors cannot be excluded. Nevertheless, the finding of a productive mesoarteritis must make one think of syphilitic disease of the aorta.

In the same number of the *Centralblatt*, Benda (page 164) discusses the etiological relationship between syphilis and aneurysms. From an exhaustive critical review of the literature and a study of 6 cases of aneurysm he concludes that the small arteries and thoracic portion of the aorta are particularly susceptible to disease in tertiary syphilis. In the aorta the process affects especially the media and adventitia, producing in these situations a true gummatous inflammation, characterized by accumulations of leukocytes, lymphocytes, epithelioid cells, and Langhans giant cells, with destruction of the tissues of the vessel wall leading to necrosis, softening, and final scar formation. These changes produce a condition particularly favorable for the formation of aneurysms. Syphilis of the smaller and medium-sized arteries do not predispose to aneurysm, since the disease process in these vessels is obliterative.

Marchand (page 197) bases his observations on a study of 23 aneurysms. In only 3 of these cases was it certain that syphilis was present. He recognizes two principal varieties of arterial sclerosis corresponding to the "A" and "B" types of Chiari. The "B" type may, particularly in young persons, be ascribed to syphilis, but cannot be held as specific for this disease, or as a gummatous formation. In his preparation, the giant cells were interpreted as foreign-body giant cells. Further, this indurating form of sclerosis may favor the development of aneurysms but the ordinary form of sclerosis is generally associated with aneurysm.

Abramow (*Virch. Arch.*, 1904, Band clxxviii. p. 406) has found in five out of six aortas from syphilitics, which he has studied, alterations which correspond to Chiari's types of mesaortitis productiva. To decide as to the syphilitic nature of this process he examined during one year all the atheromatous aortas in the material at the "Nicolai" Stadtkrankenhaus of Rostow. From this study he concludes that syphilis in the aorta, as in other organs, may give rise to gummatous processes and ordinary cirrhotic changes, but that only the gummatous aortitis may be looked upon from an anatomical standpoint as specific. The other changes analogous to those described by Chiari cannot be termed specific and may occur in other conditions.

## HYGIENE AND PUBLIC HEALTH.

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UNDER THE CHARGE OF

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**Standards of Ventilation.**—In an address before the British Medical Association, DR. J. S. HALDANE (*Public Health*, October, 1904, p. 32) asserts that, contrary to text-book traditions, an excess of 35 volumes over the normal content of 3 volumes of carbon dioxide in 10,000 of air will have practically no effect *per se* on human beings. Experiments conducted with Mr. J. G. Priestly have shown that the percentage of carbon dioxide in the alveolar air in man "is kept constant in each individual with almost astounding precision," and that, "if the inspired air contains 50 volumes per 10,000, the change in the depth of breathing . . . is quite inappreciable to the person breathing." The increase in the proportion of carbon dioxide in the alveolar air "would certainly produce marked discomfort, if it were not so easily got rid of by a very slight increase in the depth of breathing." The deficiency of oxygen in the air of rooms he regards as of equal unimportance, and the same is true of the aqueous vapor, since the relative humidity, except in extremely close rooms and in warm weather, is usually lower inside than outside. The hypothetical volatile organic matters of respired air he regards as probably non-existent, and, therefore, devoid of influence. That they cannot be of a proteid nature, as some have asserted they are, hardly needs argument, since no volatile proteid matters have yet been discovered; and that they cannot be toxic is proved by the fact that injection of large amounts of the condensed aqueous vapor of respired air produces no more effect than that of

equal volumes of distilled water. He calls attention to the fact that schoolmasters who spend their working hours in rooms in which the air is very much vitiated by respiration have a much lower comparative mortality figure than lawyers, physicians, and farm laborers, and that their comparative mortality figure for phthisis and other respiratory diseases is even lower in proportion than the general death rate. But schoolmasters are associated with children, who are very little subject to phthisis, which is more a disease of middle age, and hence there is not the danger of infection which comes to those associated in crowded rooms with adult workers. Since the danger of infection by virulent bacilli is much greater in rooms occupied by spitting consumptives, a far higher standard of ventilation is required for such places.

In place of the legal limit of 9 volumes of carbon dioxide in 10,000 of air, fixed several years ago for cotton factories only, where the air needs to be humidified, a departmental committee, consisting of Haldane and Osborn, of the Home Office, recommended, in 1902, that one of 12 volumes for daytime and 20 for night, when gas is burning, be established for workshops generally, in the belief that great improvement would thereby be effected. This recommendation was vigorously objected to, on the ground that the proposed standard was much too lax and would render nugatory all attempts to secure efficient ventilation. Haldane insists, however, that it is impracticable to make no allowance for burning gas, for, although the products of combustion can doubtless be removed by systems of ventilating pipes, such are practically never used in factories and workshops, and would be extremely troublesome and costly; and he can call to mind no gas-lighted factory, however well ventilated, where a standard of 9 volumes can be maintained after dark in winter. An ordinary gas flame consumes five times as much oxygen and produces about three times as much carbon dioxide as an adult man; and hence a maximum standard of 20 volumes of carbon dioxide per 10,000 of air after dark appears to be reasonable. The air of elementary schools appears to be fully twice as bad as that of factories; and he recommends that if a 12-volume standard be enforced in factories, it be enforced also in schools, in spite of the necessary and very considerable expense involved.

[Anybody who has had considerable experience in the examination of school-room air knows that, in spite of all attempts to keep impurities down, the carbon dioxide is commonly far more abundant than Haldane's proposed standard would permit, especially in old buildings. Repeated examination by the writer of the air of a number of old schoolhouses at different seasons of the year yielded averages which more often reached 30 than 12 per 10,000.—C. H.]

**Milk and Disease.**—*Typhoid Fever.* An outbreak of typhoid fever among factory hands, the cause of which was traced to milk, is described by DR. W. R. STOKES (*Journal of the American Medical Association*, February 25, 1905). The number of persons employed included 1500 girls and women and 400 men. The former were served with a light luncheon, which included a glass of milk, but the latter went out to neighboring places where beer could be procured. The outbreak was confined almost exclusively to the women, of whom there were as many as 200 absent at one time, but the manager believed that many were away from causes other than sickness. The milk supplied came from

a dairy where there was no history of typhoid, but bacteriological examination revealed the presence of 4,500,000 bacteria per cubic centimetre, and colon bacilli in  $\frac{1}{1000}$  cubic centimetre samples. The well, which was not protected from surface drainage, was distant about fifty feet from the privy, the box of which was full of liquid fecal matter, and close to the place where the milk was cooled. Many flies were observed about the box, and they had free access to the milk-room. The well-water contained bacillus coli and 6000 bacteria per cubic centimetre, and the ice yielded bacillus coli in 1 c.c. samples and 5000 bacteria per cubic centimetre. The milk supply was cut off, and the outbreak came to an end.

*Septic Sore Throat.* During October and November, 1903, about 250 cases of septic sore throat occurred in the Station Ward of Woking and in a district adjacent thereto. They were fairly well distributed over the ward, and inquiry by DR. R. W. C. PIERCE (*Journal of State Medicine*, October, 1904, p. 595) into their cause led to the suspicion that they were due to milk from a farm which was the common source of supply to two dealers, who, it transpired, had complained to the farmer of the ropy character of his product. The twenty cows appeared to be healthy, but four were found to have garget, their milk containing much pus and an abundance of streptococci. The supply was shut off after November 14th, and the outbreak ceased. The farmer himself had had a severe sore throat about the middle of September, and his wife, two sons, and two daughters had been similarly afflicted during October. The majority of persons affected were adults, and among these there were eight deaths attributed to the infected milk. In many instances whole families were seized, and in one house twelve of the thirteen inmates were victims. In a number of houses invaded the succession of cases suggested the probability of contact infected. The lesions varied in character and extent. Many were indistinguishable from ordinary cases of follicular tonsillitis; others were suggestive of diphtheria, and others developed into quinsy. Usually there was considerable constitutional disturbance, and a marked tendency to involvement of the submaxillary and posterior cervical glands, which remained enlarged for a considerable length of time. The lesions were not always confined to the tonsils; in some cases the pharynx and larynx were involved, making deglutition exceedingly painful and difficult. One patient, with his nasopharynx covered with a sloughing membrane, was sent to the hospital and died in about a week of pyæmia, with a post-mortem temperature of 110°. His wife was confined about the same time and developed puerperal fever, and two of his children had sore throat. Numerous victims had pain and tenderness of the joints, following the throat symptoms in from three to seven days. In five instances very severe erysipelas followed the throat symptoms, and one of these patients developed a mastoid abscess and died in about ten days from the onset.

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CEREBROSPINAL MENINGITIS.

A STUDY OF THIRTY CASES IN THE NEW YORK EPIDEMIC.

By N. B. FOSTER, M.D.,  
OF NEW YORK.

ETIOLOGY. The immediate cause of epidemic meningitis is accepted; the remote causes are known in so far as unhygienic conditions predispose to any infectious disease, but we are still in the dark regarding the portal of entry of the diplococcus of Weichselbaum into the system, and hence we are not in the position to fight meningitis on the same footing of prevention as in some other infections. In their study of the epidemic at Lonaconing, Maryland, Flexner and Barker excluded air, soil, water, and food as carriers of the infection—a position that would be held by few at present, though the contrary has not been proved. It was long since noted that epidemics of meningitis occur in prisons and barracks where crowding is a feature, and the slums of the larger cities approach to these conditions; the air, food, and general hygiene being much below that which would be tolerated in any prison even under political corruption.

The question of the contagiousness of cerebrospinal fever has been brought to the attention of boards of health by the spread of the disease in families. Three cases of this series belonged to one family, and in the last month (October) a fourth case has been reported from the same family. The first case (Case VII.) was a boy, aged six years, who was admitted to the New York Hospital on April 10, 1904, very sick from cerebrospinal fever. He died on April 11th, the autopsy demonstrating besides meningitis a purulent pericarditis. The second case, a girl aged four years, was admitted April 25th, and on April 26th the third member of this family, a

girl aged three years, was brought to the hospital. Both of these cases were mild and both recovered from their illness. The fourth case was admitted in October and died three days after admission. Osler records a family, five of whose members suffered from the disease, and Sewall reports six children in one family in the New York epidemic of 1872. Similar facts have been noted by other observers. While many feel at present that the disease is communicable, it has not been possible up to the present to gather evidence sufficient to justify that attitude on the part of boards of health. The isolation of those suffering from cerebrospinal fever should, however, always be observed as much, perhaps, for the benefit of the sick as to diminish any danger to those in health.

The winter of 1903-1904 was notable in New York for the number of cases of pneumonia and the terrible mortality from that disease. It was one of the severest winters in many years. Doubtless the lowered resistance produced by bitter cold and its attendant sufferings among the poor was a factor in the meningitis epidemic as well as in pneumonia. It has been noted in some epidemics, notably those of Hamburg and Boston, that the disease prevailed among horses as well as human beings. This appears not to have been the case in the New York epidemics, reports from the veterinary hospitals showing no increase in the number of cases of meningitis in horses. There is no evidence to show that the disease is transmissible from horse to man, or, indeed, that the disease in animals is due to the same micro-organism.

In the six months from January to July, 1904, there were 30 cases of meningitis admitted to the medical wards of the New York Hospital. Of these 18 were males and 12 females (60 per cent. and 40 per cent.). The incidence of the disease with reference to age is as follows: 12 (or 40 per cent.) were under ten years of age; there were 11 cases (36 per cent.) in the second decade of life, 2 in the third, 3 in the fourth, and 2 in the fifth decades.

MODE OF ONSET. No disease presents greater diversity in its mode of onset. The idea that there is an incubation period during which the individual suffers from some general disturbances and feels himself out of health has not been found true in most of our experience. One of the severest cases of this series was brought to the hospital in a police patrol wagon. While walking along the street, the man was seen to stumble and fall. He had a convulsion then, and was in a convulsion when first seen at the hospital. After recovering from meningitis this man told the writer that he had been in perfect health and remembered no headache until he became conscious in the hospital ward. Another case of very sudden onset resembled acute nephritis and uræmia. He was brought to the hospital late one night, with the history of having been taken ill early in the evening and having had one convulsion. The man seemed *in extremis*, Cheyne-Stokes respirations, marked œdema of

the lungs, and poor heart action. Examination of the urine was made at once; blood, albumin, and casts being found. Death occurred four hours after admission to the hospital, and autopsy showed cerebrospinal meningitis and acute nephritis. The resemblance of meningitis in adults to a uræmic state is sometimes rather close. An elderly man had been under treatment at his home for one week for what was supposed to be chronic nephritis. His condition did not improve, coma gradually came on, and he was sent to the hospital. None of the typical signs of meningitis were found, but lumbar puncture was done, nevertheless, and turbid fluid withdrawn. The spinal fluid was found to contain numerous intracellular, Gram-negative diplococci. The usual history is that while in apparent health the individual is suddenly seized with a splitting headache; delirium occurs in a few hours, rapidly increasing in intensity until the sick one keeps up a continuous talking, crying, and screaming. Convulsions occur in adults, but not so commonly as in children.

In children the initial symptoms are apt to be referred to the gastrointestinal tract. Vomiting is often the first sign, and this may be followed by a convulsion. Later it is noted that the child prefers to lie on its side and that the head is retracted. Probably due to the profound toxæmia children appear to suffer less from headache than do adults. It is certainly less marked in the epidemic meningitis than in the tuberculous form. There is often some boring of the head into the pillow and perhaps an occasional moan, but the sharp cries and periods of screaming that evidence such acute pain in tuberculous meningitis are but rarely seen in the epidemic type. A stuporous condition may prevail from the first, and becoming more profound so gradually that as death approaches it is sometimes a surprise to find the heart still acting.

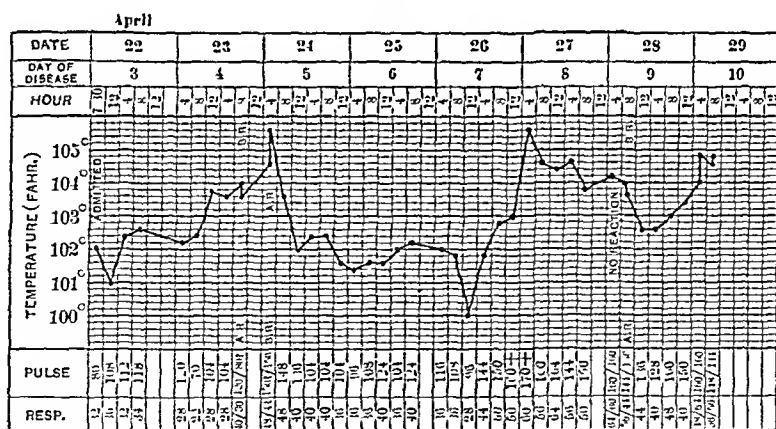
**SYMPTOMS.** Pain is a constant symptom; it may be limited to the head or may extend to the neck, back, and extremities. The headache is of the severest character, causing the patient to beat the pillow with his head and thrash the bed until overcome by exhaustion. In children a boring motion of the head and grinding of the teeth doubtless indicate pain and headache. The headache is usually referred to the occipital region, the pain extending to the neck. Sensitiveness to pressure over the cervical vertebræ is common, and in some cases pressure over the entire spinal column causes pain. Any effort to overcome the retraction of the head is resisted by the patient to the best of his power. The headache, opisthotonos, and spinal hyperæsthesia have apparently some relation to the amount of cerebrospinal fluid, for when these symptoms are very pronounced lumbar puncture shows an increased pressure in the subarachnoid space. This pressure being reduced by the withdrawal of fluid, the symptoms are almost always ameliorated.

Vomiting is an early symptom, more commonly noted in children than adults. Some gastric disturbance is often the first indication of the disease in children; in adults it may be an initial symptom or occur later in the course of the disease. We have not seen vomiting so pronounced as to interfere with recovery, as Leyden mentions in his report.

Retraction of the head was present in some degree in all cases of this series. In very severe infections in children there may be the most marked grade of opisthotonos, but the neck symptoms may, however, be very slight and cause the patient no pain. One of the earlier cases of this series came to the hospital complaining only of the retraction of his head. He had no other symptom that caused him inconvenience, and diagnosis could not have been made without examination of the spinal fluid.

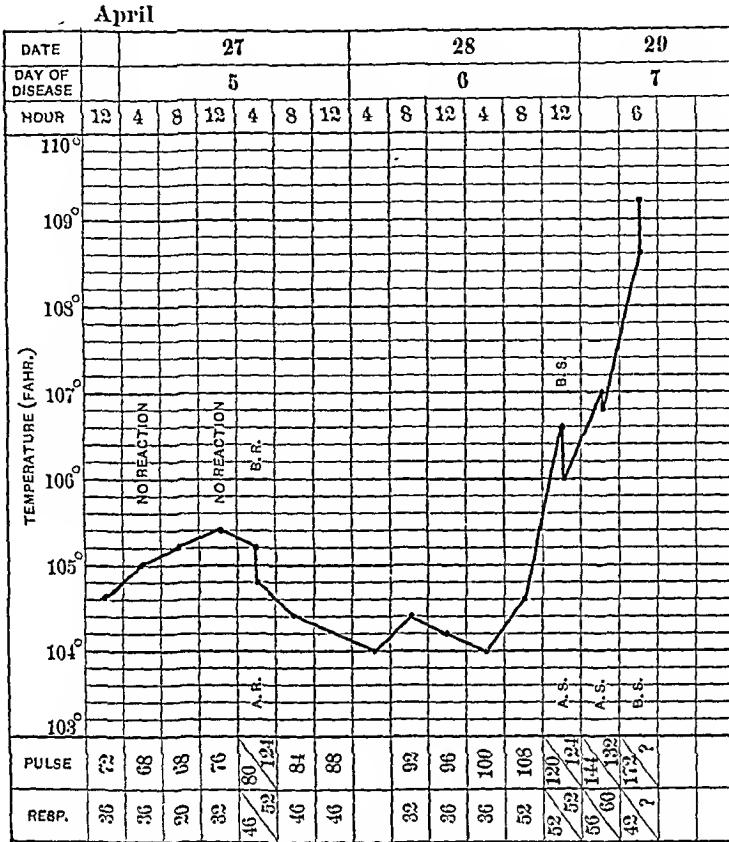
**TYPES OF FEVER.** Jackson noted early in the last century that there seemed to be no characteristic temperature in spotted fever, but not until Wunderlich studied the Leipzig epidemic of 1863 and 1864 were careful observations made on the febrile reaction of the disease. He noted a marked divergence in temperature according to the type of the disease, and suggested that this might be due to complications. Strümpel noted that there is no relation between the height of the fever and other symptoms; the severest cases may run a course of low fever or even a subnormal temperature. Strümpel suggested that this might be due to disturbances of heat regulating centre.

CHART I.



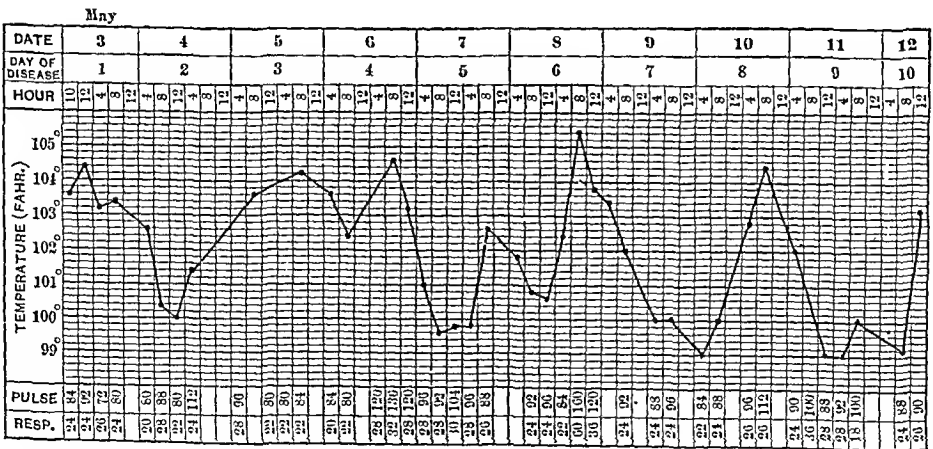
XV.), and Berg has noted that cases dying in coma have high temperatures. Those most favorable for recovery have, perhaps,

CHART II.



CASE XV. Ante-mortem reaction.

CHART III.



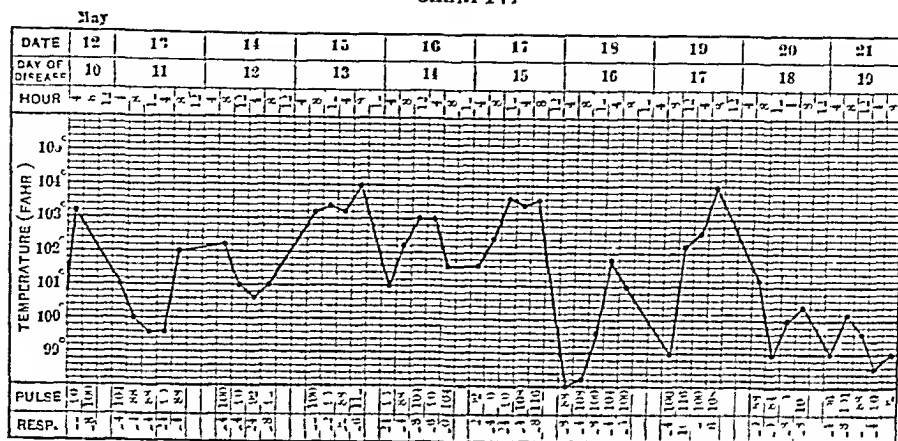
CASE XVI. Temperature normal after twentieth day. Discharged June 11, cured.

a febrile reaction ranging between 101° and 104°. It may be that the very high temperatures manifest an overwhelming intoxication, while the low fever suggests a poor reaction to the infection. The



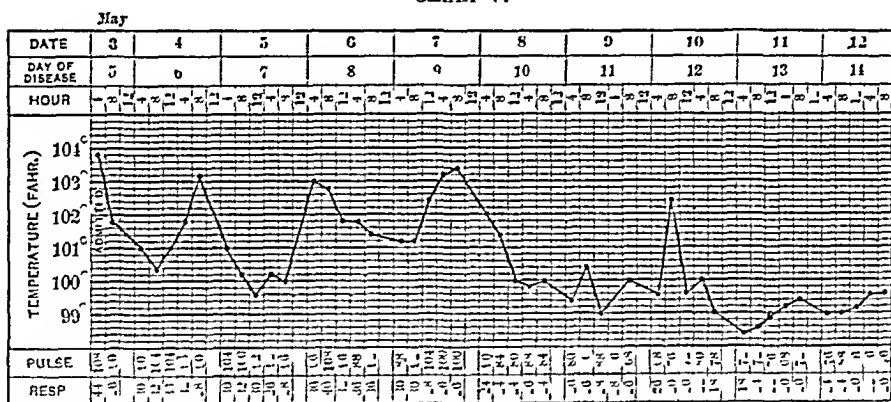
temperature curve is usually irregular, not resembling a typhoid fever chart nor yet the rises and falls of a tuberculous fever. There is sometimes a daily evening rise of temperature, as in the chart of

CHART IV.



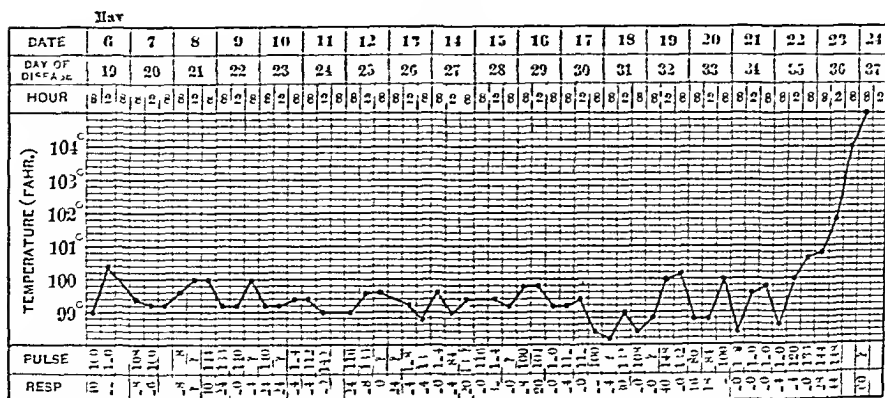
CASE XVI.

CHART V.



CASE XVIII.

CHART VI.



CASE XIX.

Case XVIII., and the excursion may amount to three or four degrees (Case XVI.). Occasionally there is an inverted type of fever. The fever may subside, the temperature remain normal for days at a time without amelioration of symptoms; this is an event which usually indicates a long course of the disease; such cases may linger on for months and concerning them it is never possible to give a definite prognosis. The pulse is relatively slow, and in this respect similar to typhoid. Cases are not uncommon, however, where the pulse remains very rapid during the whole course of the disease. Early in the sickness it is usually full and strong, but later it may be weak and often irregular. With the advent of cardiac complications such as pericarditis, it assumes the characteristics of these affections.

**SKIN RASHES.** This manifestation of cerebrospinal fever is not observed as commonly as might be expected from the name given to the disease early in its history—spotted fever. Purpuric eruptions were noted in 6 cases of this series. The rash usually first appeared as petechiæ; these sometimes enlarge and become confluent in areas several inches in extent. In severe cases these patches of purpura have been seen on the back and buttocks, having the same appearance and distribution as livor mortis. The rash is usually seen on the chest, abdomen, and back, less frequently on the extremities. Herpes occurred in 5 cases. It is much wider in its spread than is usual in pneumonia, extending from the lips, covering the cheeks even to the ears. In 1 case pustules the size of the finger-nail appeared in several places on the body and extremities. These pustules were superficial, without circumscribing induration and were not sensitive.

The pus was examined by smears and cultures, but no organisms were ever found.

**BLOOD CHANGES.** There is always an increase in the number of leukocytes, the average count for this series being 18,000. In children the leukocytosis is more pronounced than in adults, a count of 30,000 not being unusual. A differential count shows an increase in the percentage of polymorphonuclear neutrophils, as would be expected. In contrast to pneumonia there is no basis for prognosis to be elicited from the leukocyte count in meningitis. The effect of the disease on the hæmoglobin and erythrocytes is the same as observed usually in fevers, a simple anæmia of the chlorotic type depending in degree upon the length and course of the disease. Concerning the blood cultures, W. J. Elser, assistant pathologist of the New York Hospital, will publish in a later report the results of his work in this direction. He has, in brief, isolated a Gram-negative diplococcus from the blood of patients sick from cerebrospinal fever. This organism is in cultural characteristics identical with the meningococcus and is pathogenic to white mice. The blood cultures were made by inoculating broth or broth-

ascitic fluid with blood taken from the veins of patients in the manner customary in growing typhoid bacilli.

*Lumbar puncture* to secure exudate for microscopic and cultural examination was done on all cases of suspected meningitis, and the meningococcus found in the spinal fluids of all cases here reported. The technique of lumbar puncture is now too familiar to require comment. The fluid obtained is spread on glass slides, fixed and stained with methylene blue and by Gram's method. When the exudate is only slightly turbid it facilitates the examination to first centrifugalize the fluid and then examine any sediment thrown down. The character of the cerebrospinal fluid in meningitis varies from a normal colored fluid having a very slight, milky turbidity to a thick, yellow pus. The number of micro-organisms may be many or few, regardless of the appearance of the exudate. There appears to be some relation between the severity of the symptoms and the character of the cerebrospinal fluid early in the course of the disease; when there is noisy delirium or coma, and marked febrile reaction pus is usually found, but as many apparently hopeless cases make a rapid and complete recovery there is evidently no prognostic data to be deduced from the character of the cerebrospinal fluid.

**NERVOUS PHENOMENA.** Disturbance of function of the nerves of the eyes is very common. The motor nerves are the first to suffer, some involvement having been found in 30 per cent. of these cases. (1) Strabismus, either external or internal, is frequent; inasmuch as the strabismus may be external at one observation and internal at another, the cause is probably an irritation due to the intracranial pressure rather than an involvement of the nerve or nucleus in the inflammatory process, though that this does occur we know from post-mortem examination. (2) A paralysis of the external rectus of one eye and of the internal rectus of the other, causing the eyes to be turned to the side may persist during the course of the disease. (3) A lateral twitching, nystagmus-like motion of the eyes is occasionally observed. The pupils may be dilated, contracted, or normal; at times they may be unequal. The reaction to light is occasionally absent, often sluggish. We noted exophthalmos in 1 case.

Defects of vision are common, and are occasionally limited to one eye. In 1 case of this series a dimness of vision of one eye persisted for nearly two weeks after the patient was convalescent and every other symptom had disappeared. Ophthalmoscopic examination showed a slight degree of optic neuritis. Marked optic neuritis was observed in 2 cases, 1 of which died and the other made a slow recovery, his sight being good after the febrile disturbances had subsided.

Manifestation of defect in the sensory-motor are as shown in the reflexes is an early and constant symptom. If the patient is examined at the onset of meningitis the knee-jerks may be found overactive;

later in the sickness we have always found them absent. Kernig's sign is not present in young children, but in adults it is often very marked, and, in connection with the headache, may give the first clue to the nature of the disease. Kernig's sign was absent in only three of the adult cases of this series.

Cutaneous hyperæsthesia is somewhat difficult to determine because in cases that are profoundly toxic only the roughest stimulation elicits any response; where the disease is less severe and responses can be depended upon an increased sensitiveness of the skin appears to be usual. A vasomotor phenomenon noted in tuberculous meningitis, *tache cérébrale*, is sometimes seen in cerebrospinal fever. It is not a constant sign and is without diagnostic purport.

COMPLICATIONS. Various signs of extension of the infection to the eye have been noted. Conjunctivitis is an almost constant symptom according to Hirsch. Other symptoms mentioned by various observers are ophthalmia, iridochoroiditis with separation of the retina, "purulent infiltration of the eye," clouding and ulceration of the cornea, etc. Until recently ophthalmologists have held that these infectious processes in the eyes were not due to a direct extension from the central focus, but were metastatic. Councilman, Mallory, and Wright deny this. The causes of the organic changes they group under three heads: (1) Neuritis or degeneration of the nerves of the eye due to their involvement in the exudation at the base of the brain, without any extension of the inflammatory process to either the orbit or the eye. (2) The inflammation from the meninges may extend directly from the brain into the eye. (3) Neuritis of the fifth nerve with destruction of the Gasserian ganglion and consequent loss of sensation. From a post-mortem examination of the eyes in 2 cases we can confirm the second of these statements, the pia arachnoid of the optic nerve being bathed with pus along the whole extent of the nerve to the orbit. In 1 case there was purulent inflammation of the orbit and complete destruction of the eye, the cornea being wrinkled and sunken, and at autopsy the eyeball was found to be surrounded with pus, and both chambers of the eye contained some purulent fluid. In the second case purulent fluid was found in the anterior chamber and around the optic nerve; the disk was swollen and red, but the retina appeared intact. In a third case there was clinical evidence of a purulent iritis associated with some clouding of the lens. The purulent material in the anterior chamber appeared thin and gravitated to the lower side as the patient turned in bed. The signs and symptoms disappeared entirely in this case, sight being restored to normal during convalescence.

Of particular interest are the complications of meningitis in the cardiovascular system. The heart was involved in 5 of the cases of this series. On the day after admission to the hospital Case

XXVIII. presented typical signs of mitral stenosis. As there was no autopsy we were not able to determine the nature of the endocarditis.

Warfield and Walker have reported a case of acute ulcerative endocarditis due to the meningococcus. The endocarditis in their case involved the aortic and mitral valves. Pericarditis was found at autopsy in 4 cases of this series; in 2 of these the pericardial cavity contained pus which was creamy in character, easily removed from the pericardial surfaces, leaving it smooth and glistening and, with the exception of a few ecchymotic areas, of normal appearance. In this respect the pericarditis appears peculiar, inasmuch as the morbid process would give rise to no signs for diagnosis clinically. The smooth pericardial surfaces would not cause a friction sound, and the amount of pus was in each of our cases too small to be noted by signs of increased cardiac dulness. After the autopsy on the first case which showed pericarditis, every case of meningitis was examined daily by several members of the hospital staff, for any signs of pericarditis that might present themselves, but the second case escaped detection in the wards and was disclosed at post-mortem. In both of these cases the pus from the pericardial cavity showed numerous diplococci of Weichselbaum. In the other 2 cases of pericardial involvement the pericardial fluid was clear, and there was no roughening of the surfaces, but scattered over them were numerous areas of ecchymoses exactly like those we found associated with a purulent pericarditis. These ecchymoses are doubtless due to thrombosis of the superficial arterioles. Whether they are the origin of infection which results in empyema of the pericardium we are unable to state, but it would appear probable.

Lobar pneumonia occurred as a complication in 2 cases of this series. Both terminated fatally. In 1 case an autopsy was done, but cultures were not made from the lungs and the nature of the pulmonary infection is not known. Councilman, Mallory, and Wright found pneumonia due to diplococcus intracellularis in 8 of their cases. Edema of the lungs is a common complication of meningitis. It occurs usually as a terminal sign, but we have also noted it as a transitory condition in very sick patients who ultimately recovered.

Inflammation of the joints in cerebrospinal meningitis was noted by Jackson and North in their studies of the disease, and it has been a common finding in all epidemics since. In 3 of our cases there were signs of inflammation in the joints. The signs observed are those common to acute articular inflammations—swelling, redness, pain on motion, and in 1 case excess of fluid. The joints involved were the wrists in 1 case, the wrists and knees in 1, and the knees and ankles in another; one of these cases recovered. Both of the fatal cases were children. All of these cases presenting joint symptoms showed other signs of a severe infection in the fever and

mental condition. A careful study of pathology of arthritis in meningitis is wanting, and beyond the finding of pus in the joints by several observers the character of the fluid and its bacteriology is not known.

**DIAGNOSIS.** The diagnosis of meningitis in adults is usually not difficult, but in children other conditions may so simulate the picture of meningitis that an opinion is not so readily formed. Not infrequently the history and symptoms presented in sick children suggest meningitis and at autopsy the meninges are found quite normal. The two conditions which in children are most likely to lead to confusion are acute gastroenteritis and bronchopneumonia; there is no symptom in meningitis that may not be well caused by either of these conditions and the diagnosis must rest upon the results of lumbar puncture. Some observers have called attention to meningeal symptoms sometimes presented in cases of influenza; concerning this we cannot give any evidence; we have never met such cases. The differential diagnosis between epidemic meningitis and the tuberculous form is not usually difficult if the case be under observation from the onset of the malady. When, however, the case is seen in the later stages of the disease the picture presented by the two forms may be very close and here again diagnosis must be left to lumbar puncture.

Head mentions that the presence of sugar in the cerebrospinal fluid of suspected cases of meningitis is diagnostic of tuberculous meningitis. We have systematically tested the spinal fluid for sugar in all cases of suspected tuberculous meningitis and have never found it in that disease; on the other hand, we have found sugar in some conditions uncomplicated with meningitis.

In considering the diagnosis of sporadic cases of meningitis the nature of the infecting organism must be determined by microscopic methods, and in any case the prognosis is so much affected by the kind of bacteria found that lumbar puncture should always be done as a means of positive diagnosis.

The differentiation of anomalous forms of meningitis from other diseases should not be difficult. The cases sent to the hospital under other diagnoses were usually clear after careful physical examinations. The attitude in bed, the mental state, the eyes, the condition of the muscles and reflexes—these alone are usually enough to give a hint of the nature of the infection and lead one to search for confirmatory signs.

**PROGNOSIS.** The mortality has varied in different epidemics from 28 per cent. to 75 per cent.; the average mortality in the epidemics reported is about 50 per cent. The mortality in this series was 60.3 per cent. Considering the individual case it is always very difficult to form an idea of the outcome. Where coma develops early recovery is rare, and the same is true of protracted cases where the fever subsides or becomes subnormal. As has been

said above, the nature of the cerebrospinal fluid gives no data for prognosis. We have several times withdrawn fluid that was thick pus and microscopic examination revealed myriads of bacteria, recovery, however, being rapid and apparently complete.

The very interesting question of mental condition of those who recover from cerebrospinal fever we have never had an opportunity to investigate. It is well known, however, that alienists consider meningitis an important factor in the etiology of juvenile psychoses.

**TREATMENT.** No disease appeals more strongly to the physician to "do something" than does meningitis; the suffering of the diseased is apparently extreme. The young physician has constantly to keep in mind that statement of Herbert Spencer: "In proportion as the judgment is most cultivated there is least yielding to the must-do-something impulse," for only so can one avoid violating the Hippocratic maxim of treatment that the drug must do no harm. There is no method or drug that has any apparent effect on the course of the disease. Efforts toward decreasing the suffering of the patient and preserving his strength is the most we can do at present. We have said before that the patient suffering from cerebrospinal fever should be isolated; the room should have free ventilation and, considering the usual photophobia, should be somewhat darkened. An air-mattress or a water-bed is best; it makes a patient more comfortable, diminishes the danger of bed-sores, and causes less skin abrasion during the active period when the patient is in almost constant motion. Restraint is nearly always necessary to prevent self-injury, and this is best effected by passing a folded sheet around the back of the neck and under the arms anteriorly, the ends being tied to side bars of the bed. The patient may then turn and there is no restriction to respiratory movements. The ankles are thickly padded with cotton-wool and bandages passed over this and made fast to the bed.

Some very sick cases never lose their appetite, and a special diet should be arranged for such. A fever diet is insufficient; eggs and farinaceous gruels may be safely given. One of the apparently hopeless cases of this series (Case XVI.), during a convulsive period of two days, would come out of a convulsion and cry lustily for food. We have seen others of that kind. There is always an increased thirst, and the rule observed in pneumonia should not be neglected here. Give them all they will drink.

Of medicinal treatment the most important indication is for sedatives, and of these opium is doubtless best. In some cases of extreme delirium huge quantities of the drug may appear to produce no effect; bromides and chloral may be added to morphine, but our experience has been that there are cases where the delirium and convulsive seizures cannot be controlled by drugs in doses within the bounds of safety. Under such circumstances a do-nothing policy is best. The delirium *per se* is no indication for treatment

of any sort, but the ceaseless activity that attends it is very wasteful of the patient's vitality. Potassium iodide has been used largely in cerebrospinal fever, but we have never noted that it had any influence on the course of the disease.

Lumbar puncture is not only the only means of certain diagnosis in cerebrospinal fever, but we are convinced it has a therapeutic value. There is quite generally an increase in pressure of the cerebrospinal fluid, and one would say, *a priori*, that relieving this tension would add to the comfort of the patient. In all cases where the symptoms have persisted for more than a few days we have been accustomed to perform lumbar puncture every two or three days. This practice was initiated, not as an experiment, but resulted from the beneficial results observed in the early cases. The effects that we have observed are: (1) lessening the delirium when delirium was present; (2) alleviation of headache, often to entire cessation; (3) awakening from a semicomatose condition to consciousness and an ability to rationally answer questions. One lumbar puncture is not sufficient; the fluid slowly reaccumulates, marking the return of stupor and headache. On this ground Sahli has advised the use of a permanent cannula. In support of lumbar puncture as a curative measure we can offer no evidence. It is a palliative means only.

Local therapeutics was first practised by von Ziemssen, who injected weak solutions of iodine. Since then all sorts of weak antiseptic solutions have been used. In the New York Hospital lysol and collargol have been employed in a few cases without any positive result. At present there is insufficient evidence to support this measure. It has been objected to on the ground that fluids introduced in the subarachnoid space at the third or fourth lumbar vertebra would not diffuse far enough to produce any effect. That this is not the fact was demonstrated in Case XVII: of this series. Twelve hours before death 5 c.c. of cerebrospinal fluid were withdrawn for microscopic and cultural purposes and 5 c.c. of a 1 per cent. solution of collargol were injected. At autopsy collargol was demonstrated in both ventricles of the brain. It would appear, then, that there is sufficient diffusion to give grounds for local medication, but at present the evidence offered by those who have given it a trial is not convincing of its utility.

Laminectomy and irrigation were done first by Cushing. It appears more rational than any other line of treatment in such a terrible disease, but the number of cases on which the operation has been performed is yet too few to warrant conclusions.



## CROUPOUS PNEUMONIA.

AN ANALYSIS FROM CLINICAL OBSERVATION OF 991 CASES OCCURRING  
IN THE PHILADELPHIA GENERAL HOSPITAL FROM MAY 1, 1897,  
TO OCTOBER 1, 1904.

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DEMONSTRATOR OF MEDICINE IN JEFFERSON MEDICAL COLLEGE.

IN considering the following analysis of 991 cases of croupous pneumonia, observed in the Philadelphia General Hospital, it is well at the outset to understand that, owing to the unusual conditions governing the environment of these cases, the results in many particulars are not such as we are accustomed to consider as ordinarily associated with the disease. The analysis deals with the raffraff of society, the ultimate subsidence of the submerged, the physical wreck whose race of life is already almost finished by diseased kidneys, a wornout heart, an arterial system brittle to the point of breaking, or a physical system degraded to the utmost by drunkenness and the lowest forms of debauchery. On the other hand, the aged come to us in large numbers from the almshouse, where in some years croupous pneumonia has prevailed in what appeared to be an epidemic and particularly fatal form. It will be seen, therefore, that aberrant types are frequent, that complications commonly dominate the clinical picture, and that the death-rate is extraordinarily high. Be all this as it may, the present collection of cases constitutes a part of pneumonia considered as a whole, belongs to certain phases of the disease under peculiar environmental conditions, and brings before us its gloomiest and most unfavorable aspect.

In collecting the material for this report, we discovered that in many instances the data at our command were not as complete as could be desired. The cases occurred during the services of a number of the visiting staff of the hospital, and a number of different internes were concerned in the taking of histories and ward notes. The quality of the notes taken differs materially, and in some cases the facts looked for could not be ascertained. The total number of cases reported upon is, however, so large that notwithstanding the inadequacy of some of the records, the general results cannot be materially impaired.

Of the total 991 cases, 757 were males and 234 females.

The ages at which the cases came under observation, divided into decades, are as follows:

From	1	to	10	years	.	.	.	.	.	.	.	.	7
"	10	"	20	"	.	.	.	.	.	.	.	.	48
"	20	"	30	"	.	.	.	.	.	.	.	.	185
"	30	"	40	"	.	.	.	.	.	.	.	.	185
"	40	"	50	"	.	.	.	.	.	.	.	.	162
"	50	"	60	"	.	.	.	.	.	.	.	.	138
"	60	"	70	"	.	.	.	.	.	.	.	.	139
"	70	"	80	"	.	.	.	.	.	.	.	.	69
"	80	"	90	"	.	.	.	.	.	.	.	.	11

In 47 instances it was impossible to ascertain the age.

Of the total number of 991 cases, 706 were observed in the following years:

1899	.	.	.	.	.	101 cases; mortality	50 per cent.
1900	.	.	.	.	.	87 "	56 "
1901	.	.	.	.	.	138 "	50 "
1902	.	.	.	.	.	107 "	56 "
1903	.	.	.	.	.	140 "	54 "
1904	.	.	.	.	.	133 "	60 "

This shows a general mortality for the five years and nine months, the records for 1904 being taken to October 1st, of 54.3 per cent., which added to the mortality of a group of cases previously reported occurring between May 1, 1897, and January 1, 1899, and numbering 285, of which 147 died, a mortality of 51.9 per cent., results in a mortality for the whole series of 991 cases of 53+ per cent., the total number of deaths being 533. This, of course, is an extraordinarily high death-rate, and is only to be accounted for by the class of patients from which these statistics are derived. It is thus in striking contrast to the figures reported by G. W. Norris,<sup>1</sup> from a series of 500 cases observed in the Pennsylvania Hospital, of which but 125 died, a mortality of 25 per cent., which is about what is generally regarded as the usual mortality attending the disease. Osler<sup>2</sup> considers the general death-rate in pneumonia to be from 20 to 30 per cent.; above the age of sixty, the mortality ranges from 50 to 80 per cent., while in young people, the tendency is to recover, the same being the case in robust, healthy adults. As bearing out this statement he quotes the German Army statistics, which show that in over 40,000 cases the death-rate was only 3.6 per cent. As compared with these figures the death-rate of over 53 per cent. in the Philadelphia General Hospital is truly appalling, and gives some idea of the extent to which complicating antecedent conditions influence the course of the disease. In our own series of cases, also, the number observed after the sixtieth year of age, which by reference to the table above will be seen to be 229, is not sufficiently large

<sup>1</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, June, 1901.

<sup>2</sup> Ibid, January, 1897.

when compared with the total number to account for the extraordinary mortality of 53+ per cent. This high figure, therefore, could only be reached in consequence of the very high death-rate during those decades of life, when under ordinary circumstances it is low, and which so counterbalances the large mortality of the later periods of life that the general death-rate of the disease is reduced to between 20 and 30 per cent.

The seasonal occurrence in 706 of the cases was found to be as follows: January, 111; February, 119; March, 125; April, 74; May, 60; June, 27; July, 18; August, 19; September, 10; October, 30; November, 57; December, 76. Considerably more than half the cases, therefore, occurred during the cold and changeable months of the year. This, of course, is in accordance with general experience and corresponds with the conclusions reached by Anders<sup>1</sup> in an exhaustive review of the meteorological conditions influencing the causation of croupous pneumonia. We cannot but concur in the final conclusions of Anders, in that the influence of the seasons is probably an indirect one, and that the general temperature, direction and velocity of the wind, and barometric pressure, play a secondary part. It is because these seasonal conditions lead to closed doors and windows and poorly ventilated living apartments that the specific poison of the disease becomes concentrated and increased in virulence. If this be true, the inference is obvious that our strongest means of prevention are to be found in living and sleeping in thoroughly well-ventilated rooms and, in general, leading properly regulated lives.

A study of the tissue involved by the lesion in 900 cases gives some interesting results, as seen by the following table:

Right lower lobe	233
“ middle lobe	23
“ upper lobe	81
“ middle and lower lobes	17
“ “ upper lobes	26
“ upper and lower lobes	10
Entire right lung	57
Left lower lobe	204
“ upper lobe	36
Entire left lung	53
Right and left lower lobes	63
“ “ upper lobes	11
“ upper and left lower lobes	9
“ lower and left upper lobes	5
“ upper and middle and left upper lobes	4
“ entire and left upper	5
“ “ “ lower	6
“ upper and left entire	10
“ middle and left entire	1
“ “ “ lower	4
“ “ “ lower and left upper	1
“ upper and middle and left entire	1

<sup>1</sup> American Medicine, 1904, p. 407.

It will be seen by the above table that of the 900 cases the right lung was alone involved in 487 or 54.1 per cent., the left was alone involved in 293, or 32.6 per cent.; both lungs were involved in varying positions in 120, or 13.3 per cent.; lesions of the apex alone, in one or both lungs, occurred in 128 cases, or 14.2 per cent. A comparison of these figures with those of G. W. Norris, in the Pennsylvania Hospital cases above referred to, shows a most interesting approximation, thus: Right lung alone involved in 51.8 per cent.; left lung alone involved in 34 per cent.; both lungs involved in 12.8 per cent.; lesion undetermined in 1.4 per cent.; lesions of the apex alone, in one or both lungs, in 15.8 per cent. Of still greater interest is a comparison of these figures with those given by Osler,<sup>1</sup> as the result of 100 autopsies made by him in the Montreal General Hospital, as follows: Right lung alone affected in 51 per cent. of the cases; left lung alone involved in 32 per cent.; both lungs involved in 17 per cent.; and apex alone, in one or both lungs, in 13 per cent. This comparison shows a very close approximation between the clinical observations of our own cases and the post-mortem findings as reported by Osler.

Some interesting points relating to etiology were brought out in the analysis of these cases. Of the 991 cases, 104 were alcoholics, not merely those addicted to the use of alcohol, for a large majority of the cases gave this history, but the subjects of recent acute alcoholic excesses; many of these developed delirium tremens and still more presented the disease in its various atypical and grave forms. The large proportion of acute alcoholic cases, and those presenting the history of chronic alcoholism with all its incident tissue degenerations, bears not a little influence in explanation of the high death-rate of the entire series.

Traumatism appeared to have some causative influence in 7 of the cases in the series: 1. History of indefinite injury to thorax three days before onset. 2. Two days before the onset patient fell, sustaining a severe contusion of the right side over the base of the thorax, as evidenced by an abrasion of the skin existing at time of admission; lesion of the right base. 3. Five weeks before onset patient fell and injured, in a manner not stated, the left side over the base of the thorax; he had blood-spitting for two days following the accident; pneumonia of the left base followed. 4. Three days before admission patient fell down stairs, followed shortly by pain in the left side upon deep inspiration; lesion of the left base followed. 5. Five days before admission the patient fell, while drunk, against a wagon-pole, after which he experienced pain in the right side. He developed a pneumonia of the right middle and lower lobes; delirium tremens; death. 6. Three days before admission, during a drunken brawl, the patient received a blow in the left side; pneu-

<sup>1</sup> Practice of Medicine, fourth edition, p. 114.

monia, of the left base; delirium tremens; death. 7. Five days before admission patient received a moderately severe kick from a horse, in the right side; in two days he experienced pain on deep breathing; pneumonia of the right base followed.

It would seem, therefore, that in a certain proportion of cases, not large, injury, especially to the chest, bears a causal relation to the development of pneumonia; not, however, by directly producing inflammation of the lung, but by decreasing tissue resistance and raising the virulence of pneumococci already present. In a collection of 320 cases of pneumonia, Litten<sup>1</sup> found 4.4 per cent. of the cases due to injury; nor do the seven cases reported from our own series represent in all probability the total number having this history, since not being especially studied from this standpoint, in many instances the facts were not elicited, and in many others the mental condition of the patients upon admission rendered impossible the taking of a reliable history.

We are accustomed to regard pneumonia as a disease of peculiarly sudden onset, yet in a number of cases included in our series, the disease began insidiously and no rigor marked the beginning of the pulmonary lesion. These cases seemed to have a well-defined prodromal stage, which passed gradually into the stage of the fully developed disease. Thus in Case 1 the onset was preceded by pain in the left knee and heel for several days, and, although the notes did not state whether other signs of inflammation were present in the joint or not, it is not impossible that a general infection by the pneumococcus existed. 2. Pain in the eyes and headache for several days before onset. 3. "Heavy cold" for one week before onset. 4. Headache and constipation for a few days. 5. Headache and malaise for one week. 6. Headache and weakness for several days. 7. Headache, languor, anorexia, soreness in the chest, and cough for two weeks before the lesion developed. 8. Malaise and chilliness for several days. 9. Laryngitis and dysphonia for four weeks. 10. "Severe cold in the chest" for four weeks. 11. Pains in the body for several days, which finally localized in the chest in the region where the signs of the lesion were subsequently discovered. 12. Chilly sensations and general weakness for two weeks before onset. 13. Bronchitis and chilliness for one week. Where these prodromal symptoms do not point directly to the lungs it will be observed that they are such as may mark the development of any infectious disease.

A chill, of course, marks the onset of pneumonia in a large proportion of cases, and it is usually one of considerable severity; in our series of cases, it was noted as severe in 492 instances; in one case of sudden onset, but in which no chill occurred, it was apparently replaced by a severe attack of vertigo.

<sup>1</sup> Zeit. f. klin. Med., vol. xxvi. p. 182.

Pain, of the peculiar stabbing character common in pneumonia, was present in 679 of the cases. Cough was noted in 737 cases; abundant sputum in 40; very scanty sputum in 76; very tenacious in 53; blood-tinged and rusty in 537; prune-juice in 14; and absence of sputum in 123. A large majority of the cases characterized by the absence of expectoration also had no cough, and in nearly all instances were either alcoholics or very aged; the cases in which the sputum was of the prune-juice variety were the same classes of subject.

Herpes was noted in 47 of the cases, a very low percentage when compared with most statistics. If there is anything in the theory assigning to the occurrence of herpes, an indication of favorable prognostic import, the class of cases comprised in this series, and the high attendant death-rate may account for the low percentage of cases presenting this symptom. There must also be taken into consideration, in this connection, the personal equation in the taking of histories, for, as previously intimated, the notes were taken by many observers. Preble, in *Progressive Medicine* for March, 1905, quotes an article by Riehl in which the number of cases presenting herpes is given as 27 per cent. This he considers very low and quotes further statistics given by Drasche, 40 per cent.; by Metzger, 43.2 per cent.; and by Smoler, 32 per cent. Even these figures he considers underestimate the facts, and states that 90 per cent. will be found nearer right than 27 per cent. He further claims that the low percentages usually given are the result of the hidden location of the eruption in many instances and its scanty character; that when "there are but one or two vesicles, and these hidden in the moustache or within the nostrils, no note will be made of them unless they are looked for." This is not in accordance with our experience in the Philadelphia General Hospital; in the last 20 cases of pneumonia coming under our observation herpes, carefully looked for, was found in but 3 of them.

Disturbances of the organs of digestion were observed in a large proportion of our cases; vomiting was noted in 95, and nausea without vomiting in 134; anorexia, of course, was a symptom in nearly all of them. Jaundice of a severe form occurred in 9 cases. Slight icterus was frequently noted and seemed to have no bearing upon the outcome of the case, but the instances presenting the condition in a grave form developed serious nervous and intestinal manifestations and all succumbed.

Nephritis was noted in 207 cases; febrile albuminuria in 232 cases. The number in which nephritis was acute was not noted, and many of the cases presenting the evidences of this complication were doubtless acute exacerbations of a previously existing renal inflammation. The cases noted as those of febrile albuminuria were those that showed albumin without casts, the albuminuria subsequently disappearing.

The number of cases in which delirium occurred was large, 213 presenting this symptom.

The highest temperature range recorded in the 991 cases was 108, the issue being a fatal one. In 9 cases the temperature was sub-normal throughout the entire period of observation; these cases all developed uremia and all died.

In 264 cases, studied in reference to the day upon which crisis occurred, the following results were obtained:

Fourth	day	.	.	.	.	.	.	.	.	7 cases.
Fifth	"	.	.	.	.	.	.	.	.	10 "
Sixth	"	.	.	.	.	.	.	.	.	38 "
Seventh	"	.	.	.	.	.	.	.	.	64 "
Eighth	"	.	.	.	.	.	.	.	.	36 "
Ninth	"	.	.	.	.	.	.	.	.	48 "
Tenth	"	.	.	.	.	.	.	.	.	24 "
Eleventh	"	.	.	.	.	.	.	.	.	16 "
Twelfth	"	.	.	.	.	.	.	.	.	4 "
Thirteenth	"	.	.	.	.	.	.	.	.	8 "
Fourteenth	"	.	.	.	.	.	.	.	.	1 "
Fifteenth	"	.	.	.	.	.	.	.	.	4 "
Sixteenth	"	.	.	.	.	.	.	.	.	1 "
Seventeenth	"	.	.	.	.	.	.	.	.	1 "
Nineteenth	"	.	.	.	.	.	.	.	.	1 "
Twenty-sixth	"	.	.	.	.	.	.	.	.	1 "

It will be observed that crisis occurred on the odd days in 152 of these cases, and on even days in 112, a preponderance in favor of the odd days that is in accordance with general experience. The prolongation of the disease in a few of the cases is, we believe, somewhat exceptional, in 21 cases the crisis occurring after the eleventh day, and one case on the sixteenth, seventeenth, nineteenth, and twenty-sixth days respectively. All of these were otherwise typical instances of pneumonia, the disease in none was prolonged by any complication, the crisis in each occurred in a typical manner, and subsequently the ordinary rapid convalescence was entered upon.

Respirations were above forty in number in 107 cases, the maximum being 82 in a case shortly before death. The pulse showed great variety in its frequency, ranging from being uncountable in some cases to 26 per minute in one case in which, after recovery, it returned to the normal pulse frequency.

The usual leukocytosis ranged from 10,000 to 40,000. The following unusually high counts were recorded: 47,600, 49,000, 49,600, 64,000, 74,800. One case, the termination of which was in death, gave a leukocyte count of 4200. No definite relation between the degree of leukocytosis and the tendency to recover could be elicited, and high leukocytosis in cases of great gravity terminating fatally was quite as frequently encountered as high leukocytosis in cases in which the symptoms were benign and which terminated in recovery. It would seem, however, that in cases in which the symptoms are not grave a high leukocyte count is in general of

favorable prognostic import. The cases in which leukocytosis was absent, on the other hand, or which showed actual leukopenia, except in a few instances the symptoms of which were very mild, almost all terminated fatally.

In 156 cases in which the chlorides of the urine were studied, they were found to be absent in 72, diminished in 66 and normal in 18.

The following complications were noted:

	No. of cases.	Death.	Recovery.
Abortion . . . . .	1	...	1
Acute articular rheumatism . . . . .	2	...	2
Cardiac dilatation . . . . .	1	...	1
Cellulitis of neck . . . . .	2	2	
"    submaxillary gland . . . . .	1	1	
Empyema . . . . .	3	2	1
Epilepsy and typhoid fever . . . . .	1	1	1
Erysipelas . . . . .	4	3	1
Hemiplegia . . . . .	2	2	
Hæmoptysis (tuberculous) . . . . .	2	...	2
Hiccough . . . . .	2	1	1
Influenza . . . . .	4	3	1
Malaria . . . . .	2	...	2
Myocarditis . . . . .	2	2	
Pleural effusion (serous) . . . . .	6	4	2
"    "    "    and alcoholism . . . . .	1	...	1
"    "    "    and pericardial effusion . . . . .	1	1	
Typhoid fever . . . . .	4	2	2
"    "    and serous pleural effusion . . . . .	1	...	1
"    "    and alcoholism . . . . .	1	...	1
Thrombosis, external jugular, and axillary veins . . . . .	1	1	...
Uremia . . . . .	9	9	

In the following conditions pneumonia was noted as being inter-current:

	No. of cases.	Death.	Recovery.
Aneurysm, aortic . . . . .	1	1	
Acute articular rheumatism . . . . .	1	1	
Ascites (hepatic cirrhosis) . . . . .	1	1	
Exophthalmic goitre . . . . .	1	1	
Influenza . . . . .	2	2	
Mammary carcinoma . . . . .	1	1	
Measles . . . . .	1	1	
Pulmonary tuberculosis) . . . . .	3	2	1
Syphilis, acute . . . . .	1	1	
Typhoid fever . . . . .	6	4	2
Valvular heart disease . . . . .	9	9	
"    "    and nephritis . . . . .	5	3	2
"    "    and carcinoma of gall-bladder . . . . .	1	1	

TREATMENT. The course of these cases seems to have been practically uninfluenced by any particular plan of treatment. The mortality seemed to remain about the same, no matter what treatment was adopted, and all plans seem to have been employed: pure expectancy, active treatment of symptoms, cardiac tonics, such as digitalis, or the differently acting nitroglycerin, expectorants, stimulating and otherwise, counterirritation or the application



of ice, bloodletting, not as a routine, but for distinct indications, and serum-therapy, all appear to have been attended with the same general result—a mortality between 50 and 60 per cent.

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## PERIPHERAL OBLITERATING ARTERITIS AS A CAUSE OF TRIPLEGIA FOLLOWING HEMIPLEGIA, AND OF PARAPLEGIA.

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WE purpose to describe a not very infrequent but much neglected form of palsy caused by obliterating arteritis in the extremities affected. When it affects the arteries of the legs in a hemiplegic the result is a triplegia which may be thought to have been caused by cerebrospinal disease if the possibility of local vascular disease and the disability resulting therefrom are not thought of.

During the acute stage of a sudden hemiplegia caused by cerebral hemorrhage or thrombosis, but never in the slowly oncoming palsy from cerebral tumor, there is, on account of the bilateral control of movements in the cerebral cortex, a temporary lessening of power of the arm and leg on the same side as the lesion. It is also well known that in the chronic stage of hemiplegia the deep reflexes on the non-paralyzed side are often permanently increased and that even true ankle clonus may be present. This temporary partial palsy and permanent exaggeration of the deep reflexes arise without any disease of the brain and cord except that which caused the primary palsy. Occasionally, however, the disturbance of function of the leg, which on theoretic grounds should not be affected, is far greater than this, and it becomes as powerless as the other, both thighs being flexed on the abdomen and the calves on the thighs, the final result being a triplegia producing a clinical picture superficially resembling that seen when diffuse myelitis has occurred in a hemiplegic. The condition must not be mistaken for the triplegia which sometimes occurs in syphilis as the result of multiple cerebral and spinal lesions, nor for double hemiplegia or hemiplegia plus monoplegia resulting from bilateral cerebral lesions. It slowly follows a single cerebral apoplexy and is caused, as is shown by post-mortem examination, not by involvement of the spinal cord, but by disease of the arteries of the legs themselves.

The condition does not seem to be very common when the frequency of hemiplegia is considered. It never follows embolic hemiplegia in young people, but occurs only in the aged whose arteries are diseased throughout the entire body.

The history of the case we report is as follows:

W. S., a white man, aged seventy-eight years, was admitted to the Philadelphia Hospital November 16, 1904, with right-sided hemiplegia. His past history is of no interest except that he had had four apoplectic strokes. The last, and the one for which he desired admission to the hospital, occurred about six months before. While standing he suddenly fell unconscious and when consciousness returned was found to be palsied on the right side of the body and speechless. He did not improve in speech or motor power, was weak mentally, and lost control of the bladder and rectum.

**EXAMINATION.** A greatly emaciated old man with spastic paralysis of the right arm and leg. He was completely aphasic, neither speaking nor understanding speech. He made no effort to express thought by pantomime. The reflexes were noted to be increased in each leg, but nothing was said in the notes of this examination as to any loss of power in the left leg. The right pupil was a little larger than the left and both reacted sluggishly to light and convergence. All the peripheral palpable arteries were much thickened. He was bedridden.

When we saw him in January, 1905, both thighs were rigidly flexed at a right angle to the abdomen, and the calves were flexed upon the thighs. The legs were strongly adducted so that the knees could be separated only with difficulty. There was no power of voluntary movement in either leg. The muscular rigidity was so great the legs could not be straightened. The rigidity was not caused by active muscular spasm. The right arm was also completely palsied and contractured in flexion at the elbow and wrist. The knee jerks could not be obtained, but this may have been on account of the extreme muscular rigidity. The muscle jerks were absent. The plantar jerk also was absent. There was no palsy of the left arm. He did not speak at all, paid no attention to anything said to him, and gave no evidence of intelligence. He would swallow food put in his mouth. Sensibility to touch and pain could not be determined because of his mental state. He died on January 15, 1905.

The necropsy revealed chronic myocarditis with disease of the coronary arteries, marked general arterial sclerosis, chronic interstitial nephritis, and areas of cerebral softening. On gross examination of the brain there was found an extensive area of softening involving a large part of the left hemisphere. The only parts that escaped destruction superficially were the first and second frontal convolutions and the anterior portion of the third, the apex of the ascending frontal and ascending parietal, the superior parietal, the

third or inferior occipital, the lower part of the second and third temporal, and a small convolution situated in the centre of the softened area in about the position of the lowest part of the ascending parietal, which must have obtained its blood supply from a vessel coming from the interior of the brain at that point. The area of softening surrounded this spot and it is hardly possible that any fibres from it escaped destruction. The mesial surface of the left hemisphere of the cerebrum was normal. On the right hemisphere there was an area of softening involving the calcarine fissure practically in its whole length (about 3 cm.) and about 1 cm. in depth. It was entirely on the mesial surface, the lateral surface of the right hemisphere appearing normal. On the basal aspect the convolutions were normal. The arteries at the base of the brain were intensely sclerotic. On section the area of degeneration in the left hemisphere was seen to extend into and involve the anterior and part of the posterior limb of the internal capsule so that fibres from any part of the left cortex except the occipital lobe would be interrupted in some part of their course. The internal capsule on the right side appeared normal. On microscopic examination the right internal capsule was found normal by the Weigert hæmatoxylin and hæmalaun acid-fuchsin methods. The left internal capsule was largely involved in the lesion of the left hemisphere. There were a few normal fibres in the posterior part of the posterior limb, but most of them appeared degenerated by the Weigert method. The right cerebral peduncle was normal: No degeneration was seen in it by the Weigert method. Sections from the left cerebral peduncle showed the whole crusta distinctly smaller than the right and the nerve fibres of the pyramidal tract completely degenerated by the Weigert method. There was an area in the internal quarter of the crusta which was only partially degenerated. Turck's column was degenerated, showing that fibres from the second and third temporal convolutions must have been interrupted in some part of their course. Sections from the pons showed complete degeneration of the pyramidal tracts on the left side by the Weigert hæmatoxylin method. On the right side they were normal. In sections from the medulla the left pyramid was seen to be entirely degenerated by the Weigert method. The right pyramid and other parts of the medulla were normal by the Weigert and the hæmalaun acid-fuchsin method. Sections from the cervical region showed degeneration, by the Weigert method, in the left direct pyramidal tract and the right crossed pyramidal tract. The small intramedullary bloodvessels appeared very prominent in sections stained by the hæmalaun and acid-fuchsin stain because their walls were thickened. Sections from the midthoracic region were similar to those from the cervical region, the degeneration being confined to the left direct and right crossed pyramidal tracts. Sections from the second lumbar showed no other changes

than above described. In the third lumbar the degeneration in the left direct pyramidal tract by the Weigert method was very slight, but distinct. In the right crossed pyramidal tract it was much the same as in the second lumbar. In the fifth lumbar there was distinct degeneration in the crossed pyramidal tract. The bloodvessels of the pia and also in the substance of the spinal cord and medulla showed marked arterial sclerotic changes, but no signs of inflammation or round-cell infiltration. The cells of the anterior horn of the spinal cord in the cervical region were normal by the thionin stain, but they were considerably pigmented and one or two showed slight granular changes in the chromophilic elements. The cells in the anterior horn of the lumbar region, second, third, and fifth segments, were the same as in the cervical region. The optic chiasm and the optic nerves were normal by the hæmalaun acid-fuchsin and Weigert hæmatoxylin stains. In short, there was nothing in the brain or cord to explain the condition of the left leg. The cord showed only the degeneration proper to be found in the right-sided hemiplegia. The conditions under which the necropsy was made prevented an examination of the bloodvessels, nerves, and muscles of the legs; so that it would be hazardous to draw any conclusions from this case alone. Fortunately we were enabled soon after to examine a case of paraplegia surely caused by arterial disease in the legs, and in which spinal-cord disease competent to produce the condition was absent. Since the arterial condition was the same in both cases, and since there was no disease of the brain or cord competent to explain the symptoms, and since pseudopalsy is well known to be caused by peripheral arterial disease, we think it explains the first as it surely does the second case.

The history of the second case is as follows:

G., a white man, aged sixty-eight years. He was senile and could give no accurate description of his illness on account of poor memory, which he himself realized. He lay in bed with the legs flexed on the thighs and the thighs on the abdomen. The muscular rigidity was very marked. He could flex and extend the thighs and calves a little and could lift the foot a short distance from the bed, but of course could not walk. Attempts at passive movements of either leg immediately increased the rigidity, which, however, could be overcome. There was a very slight occasional knee jerk on the right side, but none on the left. The muscle jerks were absent. He had incontinence of urine and feces. Some weeks before death sensibility was normal on the legs, but whether they became anæsthetic before death we do not know. There was no deformity of the spine nor pain on pressure over it. There was slight muscular wasting in both legs. Later he developed gangrene of the foot and died February 1, 1905.

NECROPSY REPORT. The immediate cause of death was the rupture of an intercostal artery. There were also general arterial

sclerosis of high grade, general senile atrophic changes in the abdominal viscera, cardiac hypertrophy, valvular sclerosis, and coronary atheroma.

The brain, spinal cord, and pieces of the posterior tibial artery, nerve, and muscle from each side were removed and preserved in Müller's fluid. The brain was well developed and there was no atrophy or areas of sclerosis. The convolutions were somewhat flattened over both hemispheres. The dura was normal. The pia was slightly thickened, but not adherent. The arteries of the brain, especially at the base, were very sclerotic. The lateral ventricles were quite dilated. The distance between the posterior horn of the lateral ventricles and the posterior pole of the brain was only one cm.; from the lateral wall of the posterior horn to the parietal surface was 2.5 cm., and from the anterior horn to the anterior pole was 3 cm. The ependymal lining of the ventricle, especially of the anterior horn, was distinctly roughened. The cortical gray matter was about normal in thickness. The foramen of Monro was distended and the choroid plexus cystic. The basal ganglia and internal capsule were normal. The aqueduct of Sylvius was patulous, the fourth ventricle about normal in size, and serial sections of the medulla showed no obstruction in the central canal below the fourth ventricle. The cerebellum, pons Varolii, medulla oblongata, and spinal cord appeared normal on gross examination.

The cortex of the paracentral lobules on each side was microscopically normal. The pia was slightly thickened. The Betz cells contained a large but (considering the patient's age) not abnormal amount of yellow pigment situated at one pole of the cell. The chromophilic elements generally stained well, a few cells only showing a granular appearance of the Nissl bodies. The bloodvessel walls were thickened, but there was no round-cell infiltration about them in the pia or cortex. Sections from the optic chiasm and from the optic nerves appeared normal when stained with the hæmalaun and acid-fuchsin and by the Wiegert hæmatoxylin methods. Sections from the medulla oblongata stained by the hæmalaun and acid-fuchsin methods appeared normal but for thickening of the walls of the bloodvessels both in the pia and medullary substance. The anterior pyramids were well stained by the Weigert hæmatoxylin method. Sections from the cervical region of the spinal cord stained by the hæmalaun acid-fuchsin method did not show the changes found in arterial sclerosis of the spinal cord—namely, an overgrowth of glia tissue about the periphery and about the bloodvessels of the cord, with a disappearance of nerve fibres. The bloodvessels in the pia and in the substance of the cord were distinctly thickened, but there was no overgrowth of glia about them. The pia was not thickened and there was no round-cell infiltration in it or about the bloodvessels in the cord.

The Weigert hæmatoxylin method showed distinct degeneration in the inner portion of Burdach's columns and in the columns of Goll, especially in the posterior portion. The Weigert method showed no degeneration of the posterior roots and entrance root zones. Sections from the cervical cord stained by the Marchi method showed recent degeneration in the entrance root zones and in the columns of Burdach. It was very slight in the columns of Goll. Fibres entering the cord showed degeneration by the Marchi method, but posterior roots attached to the section were normal. There was no recent degeneration in other parts of the section. Sections from the thoracic and lumbar region stained by the hæmalaun acid-fuchsin stains showed the same conditions present as described in the cervical region. Sections from the lower thoracic region stained by the Weigert method showed degeneration in the posterior columns more marked in Burdach's columns and the anterior portion of the columns of Goll. The entrance root zone did not show degeneration by the Weigert method. The Marchi method showed marked recent degeneration in the columns of Burdach and in the fibres of the posterior roots after passing through the pia. The posterior roots outside the pia showed no degeneration. Sections from the lumbar region showed a diffuse degeneration of the posterior columns by the Weigert hæmatoxylin method, which, however, did not extend as far forward as the commissure or as far back as the pia. The entrance root zone and the anterior and lateral columns were not degenerated. In sections from the lumbar region stained by the Marchi method the recent degeneration was seen beginning where the posterior roots pass through the pia and extending directly to the degenerated part of the posterior column, the middle third, on each side. There was no degeneration in other parts of the section. Posterior lumbar roots, cut separately from the cord, showed no degeneration by the Marchi method. The cells of the anterior horns of the spinal cord in the cervical, thoracic, and lumbar regions were studied with the thionin stain. They contained a very large amount of pigment. Occasionally the pigment occupied the entire cell and the nucleus was not visible. The chromaphilic substance was usually well stained. In one or two cells (from twenty-four sections examined) there was chromatolysis with displacement of the nucleus to the periphery. Considering the age of the patient, the anterior horn cells may be regarded as normal. The posterior tibial nerve from the right side was almost completely degenerated. The sheath of the nerve was very thick and there was great overgrowth of connective tissue between the bundles of fibres. The nerve fibres themselves in many of the bundles had been replaced by fibrous tissue. But few normal axis cylinders were seen. There appeared to be no inflammatory process or round-cell infiltration. Sections of the left posterior tibial nerve had the same appearance as the

right. The right tibial artery showed such marked thickening of the wall that its lumen was almost closed. The left posterior tibial artery was closed by an organized thrombus. Sections from the right and left posterior tibial muscles showed great atrophy. The muscle fibres had a rounded appearance and were separated by an overgrowth of fibrous tissue. Small bloodvessels seen in the sections showed almost complete closure by the thickening of their walls. No nerve fibres were seen in the sections of muscles stained by the Weigert method. The intramuscular nerve filaments had probably degenerated completely. To sum up, there was moderate dilatation of the lateral ventricles, some degeneration of the posterior columns of the cord, great general arterial sclerosis so marked in the right posterior tibial artery as almost to occlude it, while the left was completely closed by an organized thrombus, muscular atrophy, and degeneration of the peripheral nerves. The changes in the spinal cord were not sufficient nor of a nature to have caused paralysis in the legs. The changes in the muscles and nerves surely resulted from the vascular disease. The case, then, was one of senile paraplegia caused by obliterating arteritis. This condition is not very infrequent. It may come on slowly with dull leg pains, paræsthesias, and gradual loss of muscular power, or if thrombi form the onset may be sudden and the result gangrene. In many cases in the earlier stages intermittent lameness occurs.

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## SOME PHASES OF THE NEUROTIC HEART.

BY

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To my mind there are few chapters pertaining to general medicine less well understood practically than the recognition and judicious treatment of nervous disorders of the heart. I would assign several reasons for my belief in this statement, which is the result of numerous continued observations dating back through many years. First, many of our inquiries to-day, especially those we are apt to regard as more accurate and complete, are made in dispensaries and hospitals, particularly the latter. Usually we regard a case as insufficient and unsatisfactory where an autopsy has not completed our record, or an evident and radical cure been established. In instances where the patient has been more or less of a sufferer during many years, and never seems entirely well, we have reasonable doubts, frequently, as to the accuracy of our diagnosis. This depends upon the fact that, seen at different times and under various conditions, the patient varies a great deal as to symp-

toms, and also, in measured degree, as to physical signs which are recognized. The patients who usually afford us the most satisfaction in the sense that we feel, as far as may be, we have mastered the correct interpretation of their suffering, are seen in private practice. In hospital cases we find many causes which lead to error in final judgment. For example, there is the previous history in which certain details are almost always lacking, because we cannot get at all the home habits and influences which have so much importance in fixing our opinion; in the hospital the nature of the case and treatment is not invariably the best we feel we could advise or urge. And yet we are really so handicapped by conditions of nursing, food, surroundings, arrangements, regulations, rules, etc., over which we can really have but partial control, that we become hesitating and uncertain at times about whatever is at all difficult and obscure. Again, often patients have left hospital, where they have been under observation only a few weeks or months. If they survive, they frequently pass from our knowledge entirely, and we are not at all cognizant of the future developments of the case. Even in the hospital, and when death occurs, an autopsy may not be obtained, and even if the autopsy is made very carefully, there are many points connected with the findings from the point of view of neurology of the heart, forcibly almost, which remain incomplete and unsolved. Finally, modern life, with all its many cares, worries, obligations of increasing number, has augmented the neurotic hearts many, many times, and yet rarely do we meet simple cases of the kind. Usually there is evidently present or there is reasonable doubt as to the coexistence of vascular or muscular changes in the nervously affected heart. Thus we see in advance how difficult and multiple the problem is when we wish fully to compass the so-called neurotic heart in all its detail and significance. As to its importance, particularly from the point of view of individual health and happiness, there can be no doubt. Already I have had to do with many who had been a source of misery to themselves and others by reason of a faulty diagnosis and prognosis on the part of the physician. This could be remedied only with greater care, sympathy, and knowledge. I hope what I shall be able further to say may prove useful to those who, like myself, have felt the need of more light on this interesting and important subject. The cases of neurotic heart are, in broad terms, of four kinds: First, those where there are general evidences of a condition of neurasthenia or hysteria, or other well-defined nervous disease. Second, those in which there is manifestly organic change of heart or vessels. Third, those where there is present a disease of stomach, bowels, pelvic trouble, etc., of which the cardiac disorder is an apparent reflex. Fourth, those cases in which the causes of neurotic heart are various, often not perfectly clear, and those also where the concomitant trouble is as much effect, probably,



as cause of neurotic heart. It is my intention to refer particularly in this paper to the latter class. I was called only a few days ago to see the following case:

A lady, married, aged fifty-two years, with one child grown and healthy. This patient has suffered for several years from symptoms of heart disorder, consisting essentially in palpitation, feeling of goneness around the heart, nervous dread of impending, sudden illness from heart disease. Five years ago she had what appeared to be a complete plugging of radial artery, probably due to a thrombus. Since that time she has had several attacks of temporary loss of consciousness without twitchings, foam at mouth, or biting of tongue. She suffers from atonic dyspepsia frequently, which is generally occasioned by errors of diet. Examination of heart does not reveal any organic changes. The pulse is regular with increased tension to palpation, even at times when she complains of great weakness. The urine is shown to be normal. Whiskey and ammonia suit her best, among remedies, at the time of her faint attacks. Latterly she has taken every night 10 grains of bromide of sodium to ward off attack of unconsciousness, and for two years she has had none. The frequent use of carminatives (*tinctura cardamomi comp.*), supported with cheery and hopeful affirmations, have given renewed well-being rapidly, when she was visibly affected from distressing heart symptoms (weight, oppression, weak feeling). Her flow is now irregular (every two or three months), not profuse, and unaccompanied with pain. She is generally nervous. The diagnosis in this case was neurotic heart accompanied with dyspepsia. The attacks of unconsciousness are due to stomach and heart reacting upon one another. When the patient is careful of her diet she gradually recovers and has only slight symptoms from heart. Gentle massage, a warm inland resort, and a mild alkaline water to drink, are counselled. A sojourn at Homburg seems desirable, but she prefers Aix for the summer, by reason of another's cure who is nearly related.

A young physician came under my care some years ago suffering from mental depression, occasioned by a diagnosis of heart disease made by a prominent practitioner. His local symptoms pointing to cardiac disorder were essentially slight; dyspnoea at times, palpitation, uneasiness and weight in precordial region. On physical examination a soft, blowing systolic murmur was discovered at the apex, and it was thought due to cardiac relaxation, or slight dilatation, possibly. Despite the fact he was passed as a good subject with no heart disease by a well-known life insurance company. At times he suffered from local eczema of hands and eyelids. This was cured with local treatment, apparently, and his cardiac symptoms relieved after a time with coca, guarana, and cactus. At times this patient suffered from mental depression and choking sensations in throat, which seemed of hysterical nature,

Mrs. A., who called on me January, 1904, complains of a weak heart. She is a widow, aged forty-eight years; has had *la grippe* every winter for several years. Fourteen years ago, was laid up with an acute attack of rheumatism; no pelvic trouble at present, but some years ago had ovaries and uterus removed for uterine fibroid; temperature normal; urine normal; moderate secondary anæmia. Examination of heart negative, except for weak action; pulse regular, with diminished tension. A combination of glycerophosphates of lime and soda with kola and daily massage was of service. Later, the hypophosphites with iron, manganese, and strychnine were taken, but the heart still remained weak and the anæmia unchanged. In this instance I believe the removal of the uterus and appendages was the underlying cause of nervous disorder of the heart. By suppression of coffee, taken daily several times, no doubt the heart seemed to gain strength and the feeling of weakness to disappear for a while. What is frequently true, and was in this instance, as the heart gained in strength, a slight blowing murmur was audible at the apex.

In the case of a young man who had grown rapidly, and who had an attack of pneumonia three years previously, there was complaint of heart weakness. Still, he could ride, row, walk fast, play polo, and not feel notably unpleasant effects as an immediate result. He was equipped mentally over and above the great number of men of his age, and worked hard and assiduously as a lawyer. Physical examination of heart showed diminished force, and the pulse was somewhat irregular and of low tension. He had a moderate secondary anæmia, and complained often of feeling tired. Iron and other tonics, good food, and out-door exercise did not notably improve the weak feeling at heart. After a time he disappeared from observation. Here again the weak heart action and secondary anæmia seemed to me mainly of nervous origin.

In some of these cases patients may suffer very much from palpitation, and this may come on suddenly, and apparently without provocation. Again, the throbbing and increased intensity and rapidity of heart beats may not be appreciable. In many instances notable physical exertion will not give rise to painful palpitation, although to this rule there are not infrequent exceptions. Undue and prolonged mental effort or lack of proper and sufficient sleep is a very customary source of cardiac palpitation.

It is rare to encounter marked slowness of pulse in purely nervous cases of heart disease, and usually when bradycardia is pronounced we must look for organic changes either within or outside of the heart.

The pathology of these cases is at times difficult to determine accurately, and of course many times we are compelled to fall back upon mere theory or speculation to explain symptoms. To-day the latest physiology would place the seat of cardiac automatic

action in the muscle cells of the heart, and therefore when these cells are deranged or altered we cannot but appreciate to what degree the cardiac force and movements may be affected. Singular to say, however, that in the simple nervous troubles of the heart digitalis is of little value, and tends rather to increase than to diminish functional disturbance. Inorganic or pseudoangina attacks are not difficult to determine in young people of marked hereditary or acquired nervous constitution. And where there have been overwork, excesses, stomachal derangements, combined or not with anæmia, or a marked tendency to rheumatism or gout, the diagnosis is relatively easy. Likewise, if alcohol or tobacco, tea, and coffee have been immoderately used, we can easily in most instances reach a satisfactory and correct conclusion. But in many instances in which we have to do with anginous attacks of men or women passed middle life already, with evidences of previous heart disease or arterial sclerotic changes, our anxieties are great and can only be relieved with the passage of time and the future development and outcome of the case.

In the case of a friend I was called to see two years ago, I was very much alarmed about his condition when I first saw him. He was suffering from considerable precordial pain and anxiety, his face was pale and anxious, and his movements distressed and painful. He complained constantly of inability to breathe. His heart was enlarged, with a marked, direct, and diastolic murmur at the aortic orifice; the pulse was frequent and tense. The patient was a dyspeptic, and indulged freely in tobacco. His diet was improperly regulated. He was relieved with frequent doses of nitroglycerin, digitalis, strychnine, and atropine. Two years have elapsed, and he has had no severe return, so far as I know, of what seemed at first to be true angina pectoris, and which I now regard as an accidental determination in a case of chronic cardiac disorder. Witness a case of another friend and patient of sixty years, who was of somewhat full plethoric habit, and who had a very nervous temperament, and was markedly lithæmic. His habits were exemplary. He did not use tobacco or alcohol; no syphilis or malaria. He was careful as to his diet. He worried increasingly about business matters, although his position was a good one, and the work not immoderate. He had two prolonged summer rests. His heart was seemingly normal, showed no increased size, and no abnormal murmurs. His pulse was as a rule regular and of good force, yet, from time to time, and with increasing frequency, he suffered from attacks of angina pectoris, which gradually became more and more distressing. He felt such intense anguish at times that he thought he was surely going to die, and the perspiration stood out in beads on his forehead during his attacks. Hypodermics of morphine failed finally to relieve his seizures, and nitroglycerin and strychnine could not prevent them. Finally, he had acute delirium in one

of his attacks, and died from a failing heart, despite all efforts made in his behalf. In this case autopsy showed sufficient signs of cardiac disease to render it at least probable that they gave a correct explanation of the distressing attacks of angina pectoris during life.

More or less pain and dyspnœa in connection with organic disease of the heart is, as we know, very frequent. Notably these symptoms are increased with physical exertion. They often return periodically, especially during the night, and when no physical exertion has taken place for some hours. In some instances, especially where there is greater dyspnœa and less pain, we are inclined to believe the symptoms may be of uræmic origin, so called. If the urine be small in quantity and the amount of urea excreted also slight, and if cardiac tonics are apparently of little use, and there is no pronounced heart disease, our opinion often seems warranted. In some such instances it seems as though a combined moderate degeneration of heart and arteries was the best explanation we could give. Finally, however, we should not lose sight of the nervous controlling influence of the heart. If with the difficulty of breathing and pain we have increased frequency of pulse, it seems as though the accelerator nerves of the heart had been unduly stimulated by some toxins formed within the economy, and not properly eliminated, through faulty metabolism. Again, where marked slowness of the pulse is present we feel confident that the inhibitory influence of the vagus is unduly exercised. As regards the causation, we are often obliged to recur to what at best is largely problematical, and rarely, if ever, wholly satisfactory. In one case of a professional man whom I have watched closely for a long period, the slightest emotion will cause very marked palpitation, with a sense of oppression. The heart beats at these times very rapidly and often irregularly. Not only that, but there are also occasional intermittences in heart beats and pulse, which are both subjective and objective. The dyspnœa, which comes after any sudden annoyance, care, worry, or unpleasant excitement of any sort, will also occur suddenly and at frequent intervals, and when patient is at perfect rest. It seems quite independent of food or drink. The latter, indeed, have been most carefully regulated. Prolonged rest, out-door life, and freedom from ordinary cares of life will improve the condition very much for the while, but return to previous conditions where daily little troubles arise, and very soon the patient suffers from his cardiac symptoms. With the palpitation and dyspnœa there is often a sinking sensation at the heart and a general feeling of prostration. The feeling of acute pain in the precordial region has very rarely been felt, and then only for a short time. In this case moderate, even very active, exercise out-of-doors may be, and is, indulged in with marked benefit. One exception is tennis, which seems to take away breath completely, and patient very soon

suffers very much from previous symptoms. Golf, riding, and rowing are freely indulged in, and only with good effects. The urine is usually light colored, in large quantity, and of low specific gravity. The heart has shown some dilatation for years, never growing worse, never getting smaller. There is at times a soft blowing murmur at the apex. The pulsation in the arteries of the neck is at times very marked, and the internal jugulars are readily dilated and swollen. Rarely does this patient suffer from marked dyspeptic symptoms. The bowels are regular, and the sleep quiet. Different remedies have been used at different times, some with good effect, others apparently inert. When taken for several weeks the glycerophosphates have certainly been useful. As a wonderful temporary stimulant, nothing equals the good effect of the best coca preparation. In winter if cod-liver oil and the hypophosphites be taken for several weeks, with improved nutrition, the cardiac nerves are evidently under better control. In these cases of neurotic heart the quantity and character of the urine vary considerably. Usually it is small or large in amount, of low specific gravity, with small urea elimination, and rarely contains a trace of albumin and a few casts. The latter observed facts are shown frequently, as we know, independently of nervous symptoms in many people otherwise healthy who have passed the meridian of life. Again, I have often seen urine of high specific gravity, moderate or small in quantity, with large urea output, upon cooling, throwing down a large deposit of pink urates or red crystals of uric acid. What is also to be noted is the occasional passage from one condition of urine to the other, and without adequate cause for the change. The urine is often passed very frequently, day and night, and thus causes annoyance. Sometimes frequent urination is only of daily occurrence; at night the patient is free from annoyance.

A maiden lady, aged forty-eight years, came to consult me on account of weakness and palpitation of heart. She is clerk in a trust company. She is overworked and in addition suffers from "nagging" of a man whose housekeeper she is, and from loneliness. Her menses are still regular, but rather profuse. She is constipated; suffers from dyspepsia caused by worry and rapid eating; urinates frequently and in large quantity; no fever, no malaria, no diseases latterly; operation for hemorrhoids ten years ago; mother died of uterine cancer, aged fifty-two years; father of heart disease at seventy-five years. Her flesh has increased latterly and she walks very little. When she comes up stairs, much out of breath. Occasionally vague pains in limbs or joints are relieved in a few days with salicin. She does not eat sweets or starches. Examination of heart shows it to be normal; no murmurs; urine, forty ounces in twenty-four hours; specific gravity, 1020; no albumin, no sugar; light straw color; no deposit. Improved upon strychnine, ammonia, and lavender. Glauber's salts every evening kept her bowels in good

condition, and when occasional rheumatic (?) pains occurred salicin (10 grains once a day) very soon relieved her.

The following case presents several points of interest: Young man, nineteen years old, has acne simplex; suffers from fainting attacks with almost, if not complete, loss of consciousness. Last attack took place in a crowded place, where there was bad air. Physical examination of heart shows slight thrill at apex, slight cardiac enlargement. First sound not well defined; second aortic sound not accentuated, second pulmonic slightly so; no murmurs; impulse not strong; apex not distinctly visible or palpable. Apparently in fourth space near nipple line; pulse depressible. No dilatation of stomach; nevertheless musical sound seemingly proceeding from the stomach with cardiac systole; spleen large; chest negative, although coughs a little; tongue broad and flabby; eats too much and too many things at meals; does not feel worse for physical exertion; feels well after cold sponge bath. Patient was ordered elixir strychnine, pepsin, and bismuth; small doses of creosote and elixir pepsin; regulate diet and exercise; continued care and watching. The diagnosis was hypertrophous dilatation of heart, with a condition of gastric catarrh caused by injudicious eating.

In this case I have no doubt the nervous involvement of the heart would account, in part at least, for attacks of unconsciousness. Of course, I do not make light of other conditions present.

For many years I have had under my professional care a lawyer, now forty-five years of age, bachelor. At different times he has been a sufferer from obstinate constipation, flatulent dyspepsia, and vague pains of an ambulant character, now fixed over coccyx or ischion, again in region of prostate, over appendical region, or in chest. At times he is a sufferer from neuralgic headaches. All sorts of theories have been invoked at different times to explain his sufferings; malaria, gout, neurasthenia, faulty metabolism, overwork, imprudences of diet, etc., have been sufficiently explanatory at times, and then utterly failed. His urine has shown persistent oxaluria and occasionally a trace of albumin. Latterly his most prominent, unpleasant, or even painful feelings have been connected with his heart. Marked palpitations, gone or weak sensations in stomachal and precordial areas are very evident. The heart is often rapid, tumultuous in its movements. Both aortic and pulmonic second sounds are accentuated. There is visible and forcible uplifting of chest wall at each cardiac systole. At times a blowing soft murmur is heard at apex accompanying the cardiac systole, which also occasions a musical bruit passing in the stomach no doubt, and caused by fluid and gas in a somewhat dilated organ. The ascending and transverse colon are often also evidently distended with gas. Owing to persistent pain at one time below the right costal margin, it was thought that an old adhesion, possibly perityphlitic, might explain numerous conditions which then were

interpreted, in part at least, as being of reflex origin. The main indications now being followed are regulated diet, diminished work, prolonged vacations, hepatic stimulants or correctives, and nervous sedatives. During the past few weeks all symptoms have been dormant for a time, and the heart itself more quiet, despite the fact that very marked oxaluria persists.

The treatment of these various phenomena of nervous heart is often puzzling and at times disheartening. At other times we may get rapidly beneficial effects with simple and obvious rational treatment. The good effects are not apt to be permanent, unfortunately, and frequently with little or no adequate cause the patient may again become as great a sufferer as previous to treatment. Indeed, such patients, from continuous suffering and apprehension, may become hypochondriacal, and are then a source of annoyance, trouble, and anxiety to friends and relatives. Finally, however, as nothing very serious occurs and as life survives, and despite complaints of cardiac flutterings and throbbings, insomnia and cold, chilly extremities, lack of circulation, and expressions of nerve weakness and general depression, mental and bodily, real sympathy from others is as a rule exhausted, and these patients are regarded as confirmed invalids, with innocent and much exaggerated symptoms. Proper, sufficient alvine evacuations are most essential to permanent well-being. To attain this at times is almost impossible, and we are obliged frequently to modify habits and recur to fresh prescriptions. Again, after much trouble and research we usually find some drug or combination which meets the individual requirement in this respect. Some preparation of aloes (preferably aloin) and the sulphate of soda in hot water at bed-time have been found very useful by me. The diet of course should be regulated, and sugars and starches reduced to a minimum. Whenever there is suspicion of rheumatic or gouty condition, so called, the most valuable remedy, and the one with fewest objectionable features, is salicin; sometimes a short course of it will be markedly beneficial. Massage treatment made use of daily is often largely instrumental in helping such patients toward a cure. The different preparations of ammonia, notably the aromatic spirits and the valerianate, are quieting and useful whenever the nervous symptoms are specially annoying and threatening. If the concomitant organic cardiac changes are marked, small doses of digitalis and nitroglycerin, combined and frequently repeated, work wonders occasionally. Whenever we have to do with true angina pectoris, as subsequent events prove to be the case, no medicine or treatment will cure, or even appreciably relieve. At times strychnine in moderate doses, and combined with pepsin and bismuth, has appeared to me useful in several instances. The use of iron for the condition of secondary anæmia has seemed to me almost inert, and the blood condition, whatever the precise cause of its impairment in lowered hæmo-

globin, specific gravity and color index, and moderate increase of leukocytes, has not improved. Subsequently, in one of my cases where the nerve tone was distinctly improved after months of care and treatment, the blood showed a decided increase in the amount of coloring matter and in the number of red corpuscles, an improved character of the latter, and a normal number and differential count of leukocytes. At the same time the urine analysis showed improvement by reason of a somewhat larger daily amount, a corresponding gravity (1015), and a normal excretion of urea. The favorable progress in this instance was fairly attributable to rest, massage, regulated diet, giving up coffee, and the use of valerianate of ammonia.

The evidences of slight cardiac enlargement, with or without apparent dilatation of the cavities, has remained about, if not wholly, the same during months and years of observation. I believe in some instances we obtain permanent good effects from the prolonged use of the glycerophosphates of lime and soda, combined or not with kola and calisaya. No drug has the same value at times in the control of the neurotic heart as coca. The great difficulty is to obtain an officinal preparation which has any real value. This depends upon several causes: first, the wrong leaf is sometimes used; it is gathered at the wrong season, when it is relatively inert, and does not contain much or scarcely any of the tonic alkaloids of coca. The coca leaf does not bear transportation from its native clime after being gathered, and if this is done the tonic alkaloids which it contains become changed and worthless medicinally as a nerve tonic. For these reasons, most unfortunately, if we wish to give our patients the benefit derived from coca, we are obliged to recur to the use of one or other of proprietary preparations. I should not advise, with my present acquired knowledge, the too long or too frequent use of coca in the treatment of neurotic heart. It is more particularly as a temporary help, when help, however, is most needed and sought for, that it should be used. Under these circumstances neither alcohol, ammonia, strychnine, nitroglycerin, digitalis, nor any other drug will be so soon and so distinctly valuable as coca. Even in those instances where pain, dyspnoea, palpitation; small, frequent, irregular pulse, and weak heart follow closely upon the general phenomena of acute infectious disease, such as pneumonia, typhoid fever, and *la grippe* notably, the best preparations of coca are simply invaluable. In some instances frequently repeated doses of tincture of strophanthus are temporarily even more rapidly and evidently beneficial than coca. Especially is this true in young girls suffering from primary, essential anæmia (chlorosis). In these cases I am convinced the heart muscle itself is also at fault, and requires rapid active stimulation, and in this respect strophanthus is to my mind a most useful remedy. I doubt if its value is enduring, and whenever I desire a prolonged,



continuous action in giving tone and strength to cardiac muscular fibres, I invariably appeal to small repeated doses of digitalis in some form, preferably the tablet triturates of the tincture, as they rarely occasion stomachal intolerance when properly made.

Finally, I would add that judicious use of a few antiseptic drugs, notably wood charcoal (Bellocque's), salts of bismuth, creosote, and the mineral acids, is extremely valuable whenever faulty metabolism proceeding from the stomach or intestines is clearly made out.

The following prescription borrowed from Gibson<sup>1</sup> is doubtless very useful at times for the flatulence of organic or functional angina:

R—Sp. ammonii aromat.	. . . . .	℥ xv.
Sp. ætheris comp.,		
Sp. chloroformi	. . . . .	āā ℥ x.
Sodii bicarb.	. . . . .	gr. x.
Aq. menth. pip.	. . . . .	℥ j.

Among the causes of acute symptoms connected with the presence of a cardiac neurosis I know of nothing to be avoided more than the immediate bad effects of a cold, high wind, or of wet and chilling of the extremities, especially the feet. The reflex inhibition of the heart in these instances evidently proceeds from the bulbar vasomotor centre, and passes down the vagal trunk to the heart, and notably to the coronary arteries. We can thus appreciate how it is that in true angina pectoris such effect from this or other analogous cause has been immediately or rapidly fatal. From a few facts recently observed it would appear that we may occasionally obtain the happiest relief of most threatening symptoms from the internal use of solution of adrenalin. Even in senile cases, in which the other cardiac stimulants had been used without apparent good results, and where no doubt pronounced organic changes of the heart existed, great temporary good effects upon the cardiac force and rhythm were obtained after one or more doses of this drug.

I believe in this connection we may profitably learn much from Dr. T. C. Janeway's observations in neuropathic individuals, and thus base our clinical views on one of the latest improved instruments of applied science—*i. e.*, the sphygmomanometer. Janeway writes: "I have seen markedly neurasthenic persons with rather low normal systolic pressure and diminished blood pressure. I am inclined to doubt the constancy of high tension in the neurotic." Thus we clearly see why adrenalin may be rationally of the greatest use at times. But Janeway wisely adds, "One must be especially careful not to confuse the neurasthenia, which is sometimes due to

<sup>1</sup> Practice of Medicine, vol. ii. p. 160.

NOTE.—The Morison Lectures on "The Nervous Affections of the Heart," by G. A. Gibson, in Edinburgh Medical Journal, 1902, vol. xii., and 1903, vol. xiii., are deserving of very high praise.

vascular or kidney disease, with its essential hypertension and the reported high normal readings in simple neurasthenics."<sup>1</sup>

I have found that some German observers, notably Krehl, His, Romberg, Leyden, and Martins, have made observations quite similar to those I have tried, though imperfectly, to record. It is claimed, indeed, not only that cardiac dilatation is sometimes of purely nervous origin, but also that some degree of cardiac hypertrophy may be of this provenance. It is also averred, and of this I am more and more convinced, that certain soft, blowing murmurs, which have been hitherto usually regarded as of hæmic origin, are due essentially to imperfect or irregular muscular control in the heart muscle, whether it be of walls or valves, and this again is of nervous origin.

As to those instances in which there is for many a day reasonable doubt as to the existence of a myocarditis as being explanatory of palpitations, rapidity or slowness of heart action, irregularity, intermittences, lessened force, localized pain, cardiac asthma, etc., rather than neurosial disturbances, nothing better has been said up to the present time, so far as I know, than by Dr. Herman H. Hoppe. So late as 1902 he writes as follows: "Before the diagnosis of dilatation or hypertrophy can be made in neurosis of the heart, we must carefully exclude all organic lesions, and must likewise bear in mind that we may have at the same time both an organic lesion and a neurosis. It is well to remember, however, that we may have as a result of simple neurosis of the heart undoubted dilatation and perhaps hypertrophy."<sup>2</sup>

In practice these cases are sometimes most difficult to differentiate, and careful, prolonged inquiry and observation will alone enable us to reach an accurate and satisfactory conclusion. Of course, if the patient is young and without a history of previous acute rheumatic or other prolonged febrile attacks, we may often be almost assured that no organic changes exist either in the myocardium, or ganglia, or nerves of the heart. On the other hand, if the patient be of middle life we become properly and naturally suspicious about myocarditis and sclerosis of the coronary arteries. In those instances where there has been a former severe attack of influenza, we have, as we know, a causative factor of considerable importance in producing organic nervous and muscular changes in the heart. We may then have both combined in this organ, and it becomes well-nigh impossible for weeks and months to determine what symptoms belong to the loss of nervous control and what to deficient muscular power. The correct differential diagnosis between neurasthenia of the heart and the cases of organic change becomes all important from the point of view of treatment.

<sup>1</sup> The Clinical Study of Blood Pressure, p. 257. Appleton & Co., 1904.

<sup>2</sup> Journal of the American Medical Association, May 24, 1904, p. 1346.

In the former examples there can be little doubt that life in the open air with increasing passive or active exercises (massage, resistant movements, graded hill climbing, etc.) is most useful and necessary. In patients affected with cardiac organic changes, especially if at all pronounced, the problem as to whether or no to advise exercise is fraught with risk or peril, with respect of improvement or cure. More than once I have been impressed with the importance and value of this point of view when I have considered the judiciousness of the present fashionable Nauheim treatment. There is no doubt in my mind that I have seen several examples of considerable and quite lasting improvement in signs and symptoms from a "cure" at this spa. On the other hand, I am now inclined to the belief that these were cases in which the neurosal element was predominant, although not fully recognized, and we could thus rationally account for the decided benefits obtained. In view of my own study and observations, I continue to oppose the sending of manifest cases of organic heart changes to Nauheim with the hope of remedial good effects. In general, I should expect positive harm to result, and the more energetic and prolonged the treatment, the greater the harm. Are not many cases reported by Bezly Thorne, Satterthwaite, and other warm advocates of Nauheim treatment, abroad or at home, merely cases of cardiac dilatation, and perhaps hypertrophy, largely due to functional disability of cardiac ganglia and nerves? Of course, as we now know, and as I have previously stated, automatic, rhythmic power exists essentially in cardiac muscular fibres, and yet it is clear arrhythmia, intermittences, palpitation, nervous angina, tachycardia, etc., may be largely influenced or caused by innumerable psychic and physical agencies, and even though the cardiac ganglia and nerves are purely sensory. Similarly, I am equally confident at present that cardiac bruits more or less intense and prolonged, usually however soft in character, may be wholly of nervous origin, and quite independent of recognizable blood changes, or changes in the locality and size of the heart. According to Whitaker,<sup>1</sup> while the cardiac ganglia are "denied the office of presiding over the motion of the heart, they have the higher one of perceiving the first influence of failing nutrition or toxic impression." It is readily understood that in diminished nutrition we may find the explanation of many cardiac neuroses, and also of altered activity on the part of the cardiac ganglia. (Hoppe.)

In all cardiac affections we should bear in mind constantly how difficult it is during life to determine accurately slight deviations from the normal, whether it be of valves, vessels, muscles, or nerves. On the autopsy table how often do these difficulties clear up and appear almost transparent, so simple are they and so easy at times

<sup>1</sup> American Practice of Medicine, vol. iv. Quoted by Hoppe.

of recognition. No doubt many cases I have seen might be classed as neurasthenia of the heart. In others this condition was not clearly defined, in view of certain symptoms present, and exception could be taken to it. Since reading Dr. William H. Thomson's able and exhaustive treatise on *Graves' Disease*,<sup>1</sup> and particularly what relates to cases without goitre, I have the impression that I have more than once treated a patient with persistent tachycardia and pronounced digestive disturbances, and did not recognize the nature of the case because neither exophthalmos nor enlargement of the thyroid was present. It is true that I have felt the importance for many years of rigid dietary and the use of suitable drugs to diminish or correct the effects of autointoxication from the gastrointestinal tract, in expressions of the neurotic heart. On the other hand, I am now convinced that the periodic use of a mercurial, and the employment of phosphate, sulphate, and salicylate of soda, with a tumblerful of hot water each morning, as well as insistence upon a dietary largely of fermented milk, as matzoon or koumyss, is very important, not to say essential, at times. To no one is the profession more indebted than to Dr. Thomson for numerous and convincing facts with which he has supported this view.

Dr. David Drummond has made a careful study of cardiac functional murmurs in articles of the *London Lancet*<sup>2</sup> and the *British Medical Journal*.<sup>3</sup> In one class he puts those of cardiomuscular origin. The murmurs may be, he writes, systolic, postsystolic, or even diastolic. "Some are loudest when patient is standing, and disappear when he is at rest in the recumbent posture, while the reverse is the case with others." In a few of the cases the possibility of slight hypertrophy existed. It is difficult, however, to determine the size of the heart in cases of nervous palpitation. A temporary increase of impulse and outward displacement of the apex beat "cannot be regarded as a sufficient indication of hypertrophy or dilatation." In regard to the cardiac dilatation which is occasionally clearly defined in the prolonged and uninterrupted tachycardia of Graves' disease, that I regard as a very different and distinct condition from the one I have in part studied in the foregoing paper.

In concluding this paper, I wish to say that I could have largely increased the number and variety of my cases. I have not done so for fear lest I weary my readers or hearers, and thus take from, rather than add to, the interest of my clinical report of personal observation and belief. I would specially emphasize certain facts which seem to me true, but as yet either insufficiently recorded or recognized, viz.:

1. An apparent or evident slight cardiac enlargement with or without dilatation, and it may be slight hypertrophy, occasioned by or proceeding directly from a cardiac neurosis.

<sup>1</sup> New York, 1904. Wm. Wood & Co.

<sup>2</sup> July 27, 1895, and April 10, 1897.

<sup>3</sup> November 1, 1902.

2. A condition of secondary anæmia, as shown by careful microscopic blood examination, with count and differentiation of white corpuscles, which remain stationary for a long while, despite the use of chalybeates and most rational treatment from every standpoint.

3. The absolute or relative uselessness of digitalis, notably, unless the heart muscle is involved, and even in these instances, for acute manifestations of weakness or failure, strophanthus is far more useful.

4. Impaired nutrition, at a given period, of the muscular walls of the heart under the immediate dependence, probably, of diminished nervous energy, gives rise to slight cardiac dilatation at times which subsequently, under judicious treatment, remains stationary as to amount, and becomes functionally compensated.

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## TRAUMA OF THE MESENTERY.<sup>1</sup>

A REPORT OF TWO CASES OF DETACHMENT AND ONE OF  
MULTIPLE LACERATIONS.

BY JOHN F. ERDMANN, M.D.,

OF NEW YORK,

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MEDICAL COLLEGE.

FEELING certain that no experiments upon the cadaver nor upon the fully anæsthetized lower animals can prove a theory or theories of causation in this lesion, I am constrained to present without any hypothetical considerations the histories of two cases of complete detachments of the mesentery at its intestinal border, extending for distances of five to ten inches, and one case of multiple lacerations in the peritoneal coat or coats of the mesentery without any hæmatomata associated with the lacerations. These three cases were observed by me in a period of three months, all making perfect recoveries, after being subjected to operations varying from simple suture of the lacerations to excisions of gut when complete detachments were present.

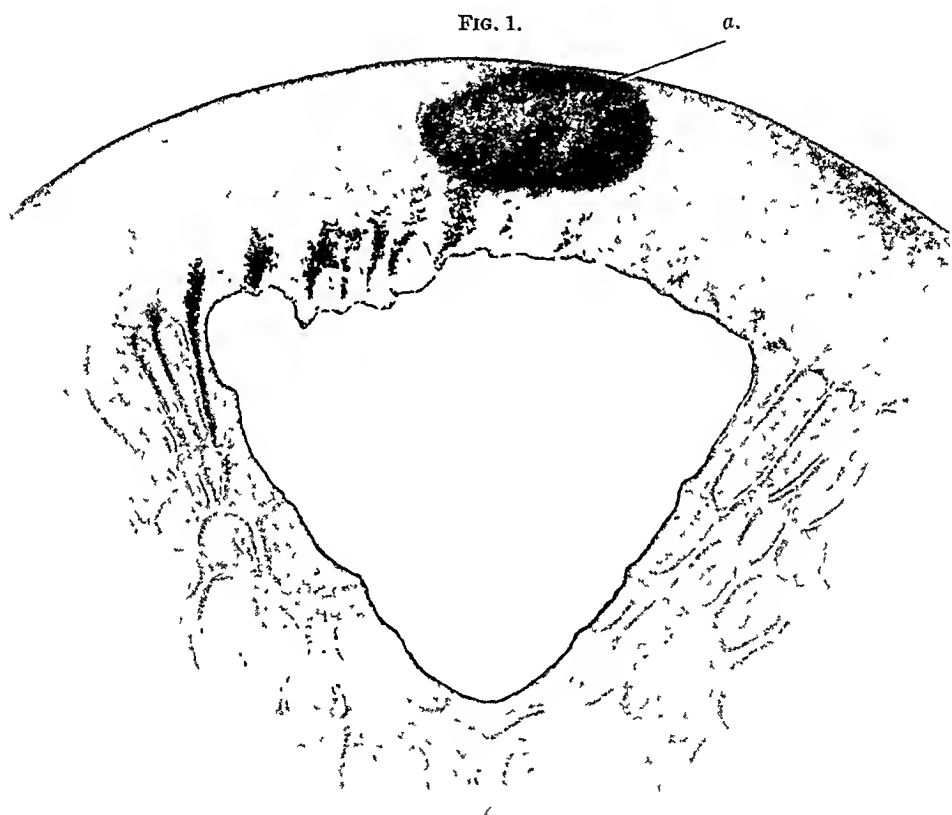
My reasons for making the assertion in the beginning of this article are governed by the differences between the abdominal muscle tone, intestinal tone, and the voluntary or involuntary movements at escape from the impending trauma in the living; as compared to the absence of these conditions in the cadaver or in the completely anæsthetized animals; also and particularly so, that even in the experiments productive of these results, we are

<sup>1</sup> Read before the Mt. Vernon Medical Society of New York, January, 1905, and the Hospital Graduates' Club of New York City, February 23, 1905.

unable to observe the exact processes taking place resulting from the applied necessary trauma.

These cases resulted from trauma that produced a compressing effect upon the abdominal contents. The detachment cases received their injuries by means of wagon wheels passing over the abdomen, while in the multiple laceration case the trauma was induced from the rear by a portion of a wall falling upon the patient's back, thereby flexing his body sharply upon a remaining portion of wall which was just high enough to make resistance at the umbilical region.

The history of the first case which I shall present is that of a boy, six and one-half years old, who was admitted to Gouverneur



a. Gangrenous area.

Hospital on February 29th last about 9 P.M. The history obtained was that sometime between 6 and 8 o'clock that evening he was run over by a wagon, the wheel or wheels passing from the anterior superior iliac spine of the left side upward and obliquely across the abdomen. A contusion about three inches long by an inch and one-half wide was seen in the vicinity of the left anterior superior iliac spine.

At 4 P.M. on the following day, when I first saw the patient, his temperature was  $101.2^{\circ}$ ; pulse, 128. The abdomen was rigid and distended; there was pain on palpation. The patient had vomited; his bowels had not moved.

Through a median incision a tear two inches long was found in the left peritoneal layer of the mesosigmoid. Further search revealed a mass of intestine, fully ten inches long, from which the mesentery was torn off, leaving a triangular gap with a base of about four and a half inches. (See Fig. 1.) The middle portion of this section contained a gangrenous area about one by two inches

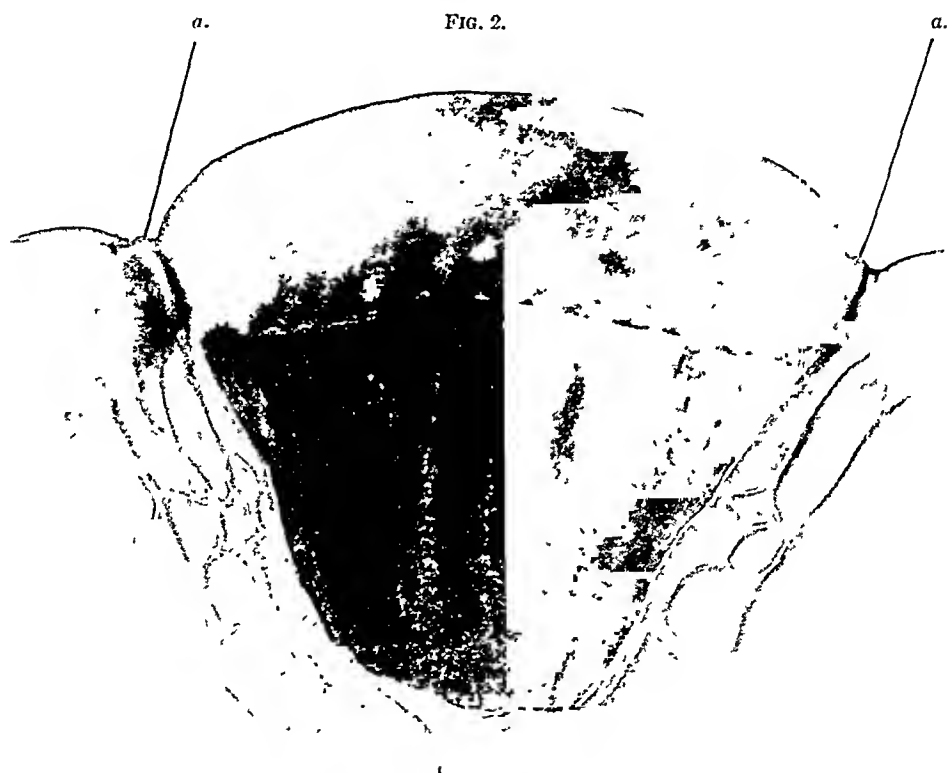


FIG. 2.

a a. Cord-like contraction.

in size. A second section of the intestine, in close proximity, was found with a triangle of its mesentery ecchymotic and gangrenous. (See Fig. 2.) The base of this was fully two and a half to three inches long. The intestine supplied by the vessels of this portion of mesentery, about five and a half to six inches long, was gangrenous in several small areas, and at each end of the destroyed mesentery the intestinal loop had a peculiar, cord-like constriction. These two sections of intestines were excised and anastomosed with Murphy buttons. The abdomen was then closed without drainage, the entire operation taking forty minutes.

The boy's reaction to the operation was favorable. The first button was passed on the ninth and the second on the twentieth day. About the fifteenth day, the patient's abdomen began to swell and his countenance became anxious. There was total obstruction for twenty-four hours; at the end of this time he began to improve and continued to do so until the 28th day of March, when some of his family smuggled fruit and cake to him, of which he ate his fill, and which was followed by profound obstruction, tympany, and vomiting. The abdomen became rigid and painful; pulse 140.

On March 30th the abdomen was again opened, and it was found that a complete separation had occurred between the ends of one of the formerly apposed and anastomosed sections. A pouch or walled-off pocket of about two inches long and fully two and a half inches in diameter was present, and by reason of overdistention this ruptured and permitted of sufficient leakage of intestinal contents to create the peritoneal manifestations. Owing to adhesions, it was impossible to bring these separated ends into the abdominal wound. They were thereupon anastomosed laterally by dropping one-half of the button into each end, then taking a purse-string suture about each end fully three-eighths of an inch away from the free edge, and inverting the open end. After the sutures were drawn tight, the button halves were forced together by nicking the gut over the stem of the female half, and then forcing the male stem, covered by the intestinal wall, into it. The cavity was wiped out, a small drain placed in the vicinity of the anastomosis, and the wound sutured. The patient began to improve immediately, and had entirely recovered by May 1st. The third button was passed ten days after its insertion.

The second case occurred August 20, 1904, a male child, nine years of age, who was run over and admitted within an hour. He was seen by me within two or three hours after the injury, at which time I found him suffering from a considerable amount of shock, with some abdominal rigidity; pain not localized to any one region. He was placed upon the operation table with a view of exploring his abdomen, with no further symptoms than those mentioned above.

As soon as the abdomen was opened, a profuse gush of blood poured out. Search of the spleen and the liver was negative; then the intestines were gone over. Practically in the middle portion of the small intestine a lesion very similar to that reported in the first case (Fig. 1) was found—*i. e.*, the mesentery was detached from the intestine with an area triangular in shape, the base of which represented about three and one-half inches in length. Seven inches of the intestines were excised and an anastomosis made by means of the Murphy button. Button passed within a period of twelve days. The patient made an absolute recovery.



The appendix was excised at the same time the anastomosis of the intestine was made.

The case of multiple lacerations occurred in an adult male who received his injuries while tearing down a brick-and-stone wall.

V. M., aged twenty-five years, entered my service on August 8, 1904, stating that while at his portion of a building which was being razed he was struck on the back by a section of falling wall, causing him to bend forward sharply upon a bit of brick-and-stone work about two and a half to three feet high, and that this was just high enough to strike his umbilical region. When removed from the debris he suffered pain of a very marked degree in his abdomen and was unable to move. He was received at the hospital at 12.30 P.M. in the following condition:

Well nourished; shock well marked; complaining of abdominal pain and tenderness; a trace of blood found in the urine; no vomiting; air hunger; blanched lips; restless; general abdominal rigidity, most marked in the hypogastric regions; tenderness also general and more defined in the hypogastric regions; no tympanites; no dulness and no mass felt. A very large and extensive area of ecchymosis was present in the left groin, running down to the outer side of the thigh; temperature, 101.5°; pulse, 124; respirations, 32.

I saw him nine hours after his injury, at which time no change had taken place in his abdominal symptoms, but his temperature had fallen to 98 $\frac{4}{5}$ °; pulse to 96, and respirations had risen to 44. A median incision was made below the umbilicus. Upon opening the peritoneal cavity a large quantity of free blood and some clot were found, enough to cause a hurried search of the liver and spleen; these were found intact. The abdomen was flushed with saline solution and sponged out, and then the intestines were gone over. Fully twenty lacerations of the mesenteric peritoneum were found, from the size of a ten-cent piece to that of one five inches long and three wide in the mesosigmoid; these were sutured with catgut. A long rupture of the peritoneal coat of a section of the small intestine was also sutured. The space of Retzius was filled with blood, while the pelvic peritoneum in the left side and extending up to the left kidney was pushed forward by extravasated blood. The kidney upon palpation seemed intact. No urine was discovered in the prevesical space. After flushing again with salt solution the peritoneal cavity was closed, a drain put into the space of Retzius, and the abdominal wound closed. There was a temperature of 98 $\frac{4}{5}$ ° to 100° for eight days, after which time the recovery, although slow, was positive, he being discharged at the end of five weeks.

In all abdominal contusions I make it a rule, if when seen the patient has any abdominal rigidity or pain, with or without evidences of blood by vomitus, rectum, or bladder, that a "*waiting for further symptoms to develop policy*" is wrong, and proceed to do an exploration. Cases seen within the first hour or two very fre-

quently are in such deep shock that some of these symptoms and signs may not be obtained. I then take the history of the injury into consideration and explore immediately if the injury has been due to a fall from a considerable height or if the vehicle or body producing the blow was of fair weight. By adhering to this rule in a period of four weeks I opened the abdomen successfully in the additional cases, all under ten years of age, finding the following:

1. Rupture of the spleen; sutured; recovery.
2. Rupture of the liver; packed; recovery.
3. Rupture of the internal coats of the stomach, evidenced by two large hæmatoma, in its wall, and accompanied by vomiting of pure blood. Recovery.
4. One of my associates, Dr. J. E. Kelly, assisted by myself, operated in one case of ruptured and fragmented spleen, doing a splenectomy with recovery.
5. One of our assistants, Dr. A. E. Sellenings, operated in a case of ruptured liver, packing, with recovery.

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## REPORT OF A CASE OF AN EXTENSIVE BURN OF THE THIRD DEGREE.

BY ARCHIBALD M. FAUNTLEROY, M.D.,

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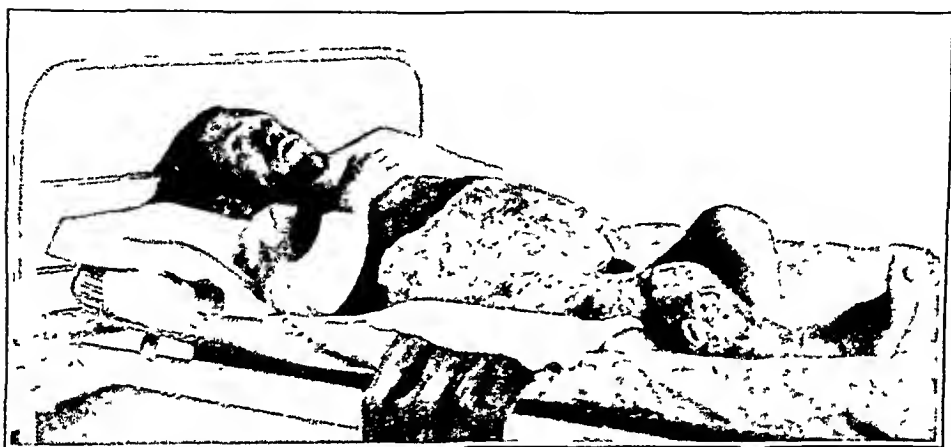
THE case is that of Moses Seattle, an Indian dwarf, the last of the tribe of Seattle, and the grandson of the famous Indian chief, Seattle, for whom the present city of Seattle is named. He was thirty-four years old, a trifle over four feet high, and had a local reputation for consuming large quantities of "fire-water" whenever it was within his reach.

The history of the accident is rather obscure, but from the statements made by the patient before death, it is believed that he, in company with a few others, was drinking in a small hut not far from the Indian Reservation at Port Madison, Washington, when he became very much under the influence of the liquor and fell asleep. While he was in this condition the small house caught fire, presumably from the fire on the hearth, and the only thing the patient remembered was suddenly finding himself struggling through the flames in his effort to escape (Fig. 1).

This happened on the night of February 4th, and when found, two days later, he was brought to the town of Charleston, just outside the navy yard, and deposited in a barn. Hearing of his condition, I went out to see him on the morning of February 7th, and found him in a very bad way. After removing the dirty cloth cover-

ing the burn, I found that the latter was of the third degree, and included nearly all of the skin over the abdominal area from the seventh rib downward. The outer surface of the right thigh and buttock and portions of the right leg were also deeply charred. The dorsal surface of the penis was involved, and a circular wound, an inch in diameter, was found just below and to the right of the umbilicus and penetrating almost to the peritoneum. The latter wound is supposed to have resulted from falling on the sharp point of something in his effort to escape. He presented evidence of still being under the influence of liquor, and under his coat, which was used for a pillow, was found a pint-flask about three-quarters empty.

FIG. 1.



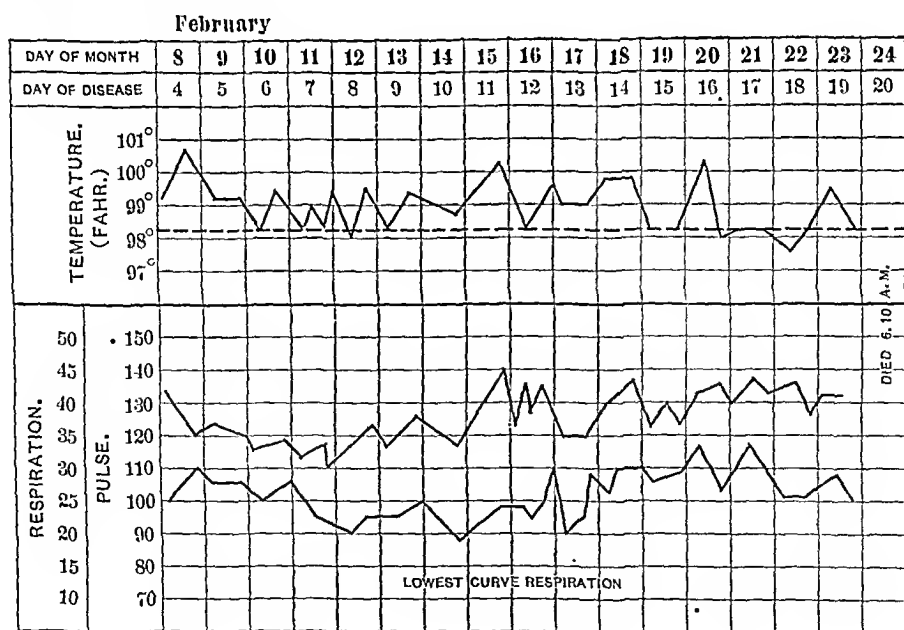
Just before my arrival a doctor in the neighborhood had administered two doses of morphine,  $\frac{1}{4}$  grain each, and the patient was comparatively free from pain. His pulse when first seen was 130, weak and irregular, but considerable improvement was noted after a pint of black coffee had been introduced into the rectum. Adjoining the stable was a small stove-heated room, which was pressed into service as a dressing-room. Here the burned area was thoroughly washed with soap and warm water, and boric-acid ointment applied. Lint and cotton completed the dressing.

After rendering first aid, an effort was made to interest the people of the neighborhood in behalf of the patient, but no one would receive him; so, for the present, there was nothing to do but to continue treatment in the barn, in which there were also quartered some five or six horses. He was made as comfortable as the unwholesome conditions would permit, and, after an injection of  $\frac{1}{20}$  grain of strychnine, he was left in charge of Frank N. Kannapell, the hospital steward from the U. S. R. S. *Philadelphia*, whose untiring attention to the sick man is worthy of note.

I was summoned from the ship about 4 o'clock in the afternoon of the same day, with the information that the patient was dying.

Having provided myself with the means for giving an intravenous infusion of normal salt solution, I hastened to the barn and found the patient apparently in a moribund condition, the pulse being so rapid that it could not be counted. Strychnine,  $\frac{1}{20}$  grain, was administered, and, after a hurried effort to sterilize the left elbow, the median basilic vein was opened, and a little over a pint of normal salt solution introduced. The patient's condition began to improve almost immediately, and before I left the barn his pulse was 130, regular, and of perceptible volume. He remained in the barn overnight in charge of Hospital Steward Kannapell and Hospital Apprentice Houser, who alternated in standing watch by the sick man, and two doses of strychnine,  $\frac{1}{20}$  grain each, were administered during the night.

The next morning, February 8th, Surgeon D. N. Carpenter, United States Navy, in command of the Naval Hospital, was communicated with, and consented at once to admit the patient to the hospital. His condition being favorable, he was removed to the hospital on a stretcher and placed in a boric-acid bath (3 per cent.), which was maintained continuously at about 38 C., and the dressing allowed to soak off. He remained in the bath for ten consecutive days, being only removed now and then to allow the tub to be cleaned, and each day the wound was examined and portions of the sloughing tissue removed. The accompanying chart shows the patient's temperature, pulse, and respiration during his stay in the hospital (see Chart).



On the second day he became tympanitic for the first time, and this condition was one of the distressing features of the case throughout his illness. At first the passage of the rectal tube and the intro-

duction of an enema of salts, glycerin, and turpentine brought away large quantities of gas and some fecal matter. Later on we found 2 drops of turpentine administered by the mouth three times a day proved very effective in preventing intestinal fermentation and keeping the bowels open. The kidneys were closely watched each day, and though, as a rule, the output of urine was found satisfactory, toward the last albumin was present, sometimes in quantity.

His pulse for the first seven days showed no signs of impending danger, but on the night of February 15th it reached 140, and became very weak and fluttering. A little over a pint of normal salt solution was again introduced into his venous system, this time through the median basilic of the right elbow: The patient revived and was put back into the tub in fairly good condition. Now and then throughout his sickness he received hypodermic injections of strychnine and brandy.

When first placed in the bath the patient was restless and unable to sleep, and, at times, in considerable pain. This condition was met with morphine, from  $\frac{1}{8}$  to  $\frac{1}{4}$  grain, but it was recognized from the first that if the atony of his bowels was to be relieved, he should be allowed only the minimum dose consistent with the pain present. He would sometimes go for whole days and nights at a time without requiring it.

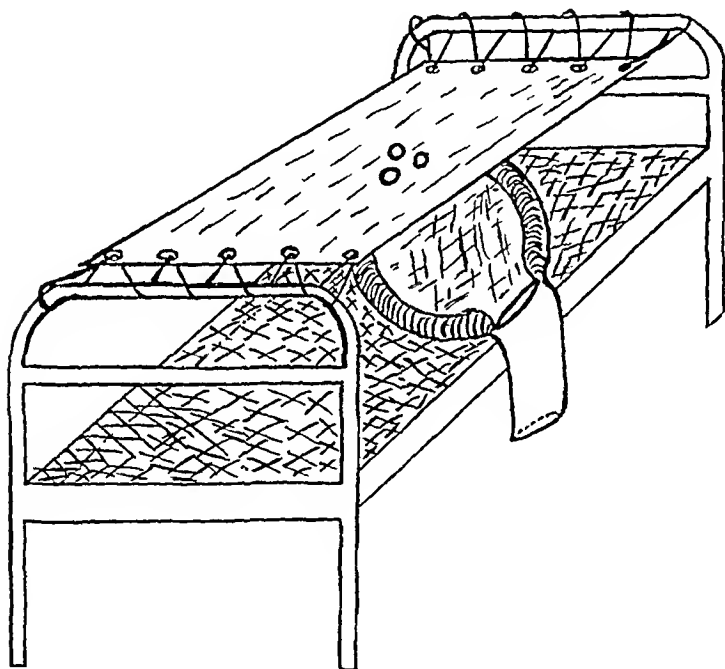
His food consisted principally of milk, beef-tea, albumen-water, orange-juice, and, at times, egg-nogg or brandy and milk. The amount of whiskey consumed per diem was gradually increased, as it was thought from his previous habits his system would miss the sudden withdrawal. The patient's marked dislike for milk and the unsatisfactory rectal feeding led us at times to deviate from the above diet, such as ordering milk-toast or very soft eggs, but it invariably resulted in distressing tympany. At one time the distention was so great that the liver was pushed up so far as to considerably embarrass the heart and respiration.

When the sloughing process had manifested itself in earnest, the patient was removed from the tub and continuous warm bichloride irrigation, 1:5000, resorted to by allowing the warm solution to trickle upon the compresses. A serious objection to this technique was that it kept the patient awake and but partially covered, and, on account of the sinking in of the middle of the mattress, caused the accumulation of the solution in the rubber pad under the patient. We hit upon a device which seemed to obviate these difficulties very nicely. It consisted in removing the mattress and stretching a piece of heavy canvas across the bed, about a foot and a half above the springs, and lashing the ends of the canvas to the top of the head-piece and foot-piece, respectively. Three small holes in the centre of the canvas allowed the solution to drain off at once into the rubber pad which was placed upon the springs below the canvas (Fig. 2).

In addition to this a fenestrated rubber tube was incorporated in the compresses over the wound and secured with a few turns of a roller bandage, and, after passing through a small hole in the blanket, communicated, by means of a short glass tube, with the rubber tubing leading from the irrigator. In this way the patient was relieved of the annoyance of the drop method, was completely covered, and the dressing over the entire wound kept moist. The patient expressed himself as being perfectly comfortable, and shortly afterward passed into a sound sleep, from which he awoke feeling much better.

The amount of skin involved was just about one-half of the body surface, if anything a little more, and he was apparently doing remarkably well for the extensive injury he sustained, but at 6.10

FIG. 2.



A.M., on February 24th, he suddenly expired, having been in the hospital sixteen days. The nurse on watch stated that the patient was talking cheerfully a few moments before, when he suddenly noticed the change in his condition, which proved to be death.

*Autopsy*, 1.55 P.M., February 24, 1905. Body a trifle over four feet long and somewhat wasted. Rigor mortis well marked. Muscular development good. Deformity of extremities and head (ostitis deformans or rachitis). Granulating surface of extensive burn covering entire right abdomen, pubes, and dorsal surface of penis. Right buttock and loin, as far as spine, involved. Burned area extending irregularly over left abdomen. Also over upper and outer surface of right thigh and leg. A few sloughs remain, but on the abdomen effort to heal is seen along the edges, which are covered by

young skin extending one-half to one inch on to the surface of the burn.

*Thorax.* Bloody exudation (about 500 c.c.) in both pleural cavities. Lungs normal, except for slight adhesions of the right lung. Pericardial fluid normal.

*Heart.* Left ventricle slightly hypertrophied. Right ventricle dilated, showing fatty changes in muscle. A large white ante-mortem clot occupying the ascending aorta and extending into the arteria innominata, bifurcating into left common carotid. Valves of heart normal.

*Abdomen.* Large and small intestines markedly distended with gas, and walls thin. Upper portions of small intestines congested and about 1000 c.c. of greenish exudate in peritoneal cavity. Parietal peritoneum beneath burn shows, macroscopically, no exudate or inflammatory change.

*Stomach* distended, but apparently normal. Duodenum congested but no *ulcers* or evidence of *marked inflammation* found, save for the adhesions of omentum to stomach, duodenum, and spleen.

*Spleen.* One-half usual size, but apparently normal.

*Kidneys.* Enlarged. Evidence of fatty changes. (Diffuse nephritis.)

*Liver.* Enlarged and fatty. Pushed up against diaphragm and encroaching considerably upon the heart and right lung.

The post-mortem findings, including a large white thrombus occupying the ascending aorta and extending into the arteria innominata, indicate that death resulted directly from asthenia due to the sudden embarrassment of an already overtaxed heart.

This was brought about by a rapid distention of the stomach and intestines with gas, pushing up the liver and diaphragm, and thus seriously hampering the heart's action, which also had to cope with the large ante-mortem clot in the aorta. The hypertrophied left heart had compensated, as far as possible, for the extra work thrown upon it by having to force the blood passed the large thrombus, but being already weakened, and finding itself suddenly in very cramped quarters, it was unable to keep up the struggle, and hence collapsed.

The continuously rapid pulse is also explained in that only a relatively small quantity of blood could be forced past the thrombus at each contraction of the ventricle, and hence there had to be a greater number of contractions to make up for the lack in volume that passed through the aorta during systole.

Had not the thrombus been present, it is reasonable to predict that the patient would have recovered, as far as the immediate results of the burn were concerned, although considerable skin-grafting would have been indicated for a complete recovery.

A review of the case presents many instructive points, which are also confirmed by the writer's previous experience with a number

of extensive burns resulting from the explosions on the U. S. S. *Massachusetts* and the U. S. S. *Missouri*.

1. All extensive burns should be treated, if possible, by the continuous warm bath. This method is very restful to the patient, relieves the existing shock, and attention can be given to the burned area without handling the patient or removing dressings, both of which operations are always attended by more or less shock and no little pain.

2. When the sloughs have begun to separate, some form of more active continuous antiseptic irrigation, preferably aluminum acetate, is indicated. (The aluminum acetate could not be obtained for this case, and corrosive sublimate was used instead.)

3. The apparatus mentioned above is recommended as meeting all the requirements. The patient rests comfortably upon the stretched canvas, and the solution does not accumulate beneath him. The fenestrated tube has obvious advantages over the continuous drop method.

4. While food is essential, it should be strictly liquid, and given in small but repeated doses. For the accumulation of gas in the intestines, which almost invariably occurs when the abdomen is involved, turpentine, in small doses, is strongly recommended, though the kidneys may be slightly diseased. The rectal tube is, of course, a useful adjunct.

5. For the shock, which is always present in extensive burns, besides the well-known methods for combating it, the intravenous infusion of normal salt solution will give oftentimes miraculous results.

6. Extensive burns, of even over one-half the body surface, should not be despaired of, as I am of the opinion that heretofore the profession has been too prone to regard as hopeless a burn involving extensive areas. As a result of this, we are liable to neglect, or regard as useless, some of the methods and technique which, at least, should be given a fair trial when it is possible to do so.

In concluding this paper, I wish to state that Surgeon D. N. Carpenter, at whose suggestion this report is made, was associated with me throughout in the management of the case. That the patient lived as long as he did is due to the praiseworthy promptness with which he was admitted to the hospital by Dr. Carpenter, as well as to his valuable suggestions and judgment in the conduct of the case.



# ACUTE FLEXION (JONES' POSITION) IN THE TREATMENT OF SUPRACONDYLAR FRACTURES OF THE HUMERUS.

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(Communicated to the Medical Society of Chihuahua, Mexico, February 10, 1905.)

If the fragments in any case of fracture can be accurately reduced to their normal position and apposition maintained, the advisability of dressing the affected limb in that position should not need to be demonstrated. Other things being equal, that position of the limb which keeps the fragments in correct position will be less apt to result in subsequent loss of function than will any other position.

These remarks, it seems to me, apply with special force to fractures about the elbow-joint. In these injuries there is often considerable difficulty in accurately reducing the fracture, and there is usually still greater difficulty in maintaining the correct apposition of the fragments. Ankylosis, complete or partial, and loss of the carrying angle ("gunstock deformity") are the results which are prone to follow neglect to secure either of these conditions.

In supracondylar fractures the deformity almost invariably consists in a posterior and upward displacement of the lower fragment, the injury being the fracture by extension described by Kocher, and the line of fracture extending from above downward and forward. The fracture by flexion, in which the line of fracture extends from above downward and backward, and in which the lower fragment is displaced forward into the soft tissues on the anterior surface of the elbow-joint, is a very rare injury. Mouchet<sup>1</sup> did not observe it once among 61 cases of supracondylar fracture.

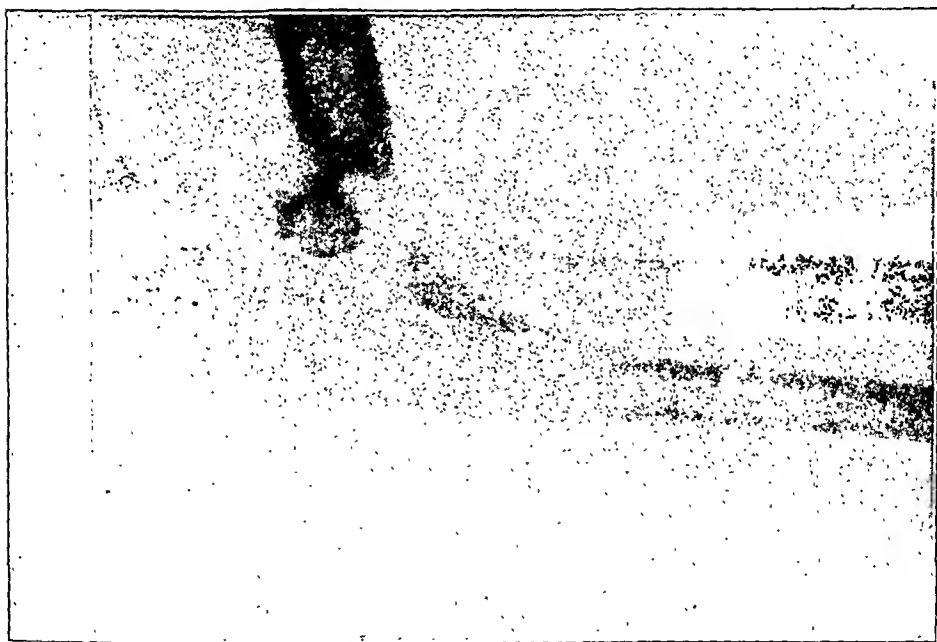
In a recent case of supracondylar fracture of the left humerus I had good opportunity to observe the effects of the position of the forearm on the fragments. As is well known, the portion broken off the humerus moves in practical unison with the forearm, the movements of the elbow-joint being in abeyance.

Ella McG., aged nine years, was brought to the dispensary of the Episcopal Hospital on the evening of November 27, 1904, within a few hours of having fallen from a chair to the floor. She had landed on the palmar surface of her left hand, which was over-extended at the time, and she complained of an injury to the elbow

<sup>1</sup> Gaz. des mal. enfant., Paris, 1904, vi., 153.

joint. The joint was very much swollen, but a supracondylar fracture was suspected. The limb was dressed by the resident surgeon, Dr. Walker, on an internal right-angled splint. A skiagraph (Fig. 1) was made by the hospital skiagrapher, Mr. Riegel, the next morning before the child returned to the dispensary. When I examined the patient at my morning visit, I found the elbow extremely swollen, but could detect no bony deformity. The extent of the swelling may be perceived by comparing the shadows cast by the soft parts of the arm in Figs. 1 and 2. The dressing was reapplied, and the child directed to return the following day. By this time the skiagraph (Fig. 1) was available, and

FIG. 1.



Eighteen hours after injury.

confirmed the diagnosis of supracondylar fracture. The youth of the patient is indicated by the separate shadows cast by the epiphyses of the olecranon and of the head of the radius. The lower fragment was seen to be still posterior, and tilted upward by the action of the triceps. In accordance with the indications, the forearm was acutely flexed on the arm into Jones' position, and maintained by the usual bandages, the wrist being slung close to the patient's neck. The swelling was still very great, and the forced flexion caused the child some pain; but I was careful to see that the radial pulse was not obliterated, and the pain ceased in a short time, and never recurred throughout the course of treatment.

To determine whether the desired result had been obtained, a skiagram (Fig. 2) was made the following day, December 1st. The decrease in the swelling and the very satisfactory position of the fragment are well shown. Thereafter the bandages were removed every third day, the elbow extended sufficiently to unfold the cubital crease, which was then washed with alcohol and dusted with boric acid powder, and the acute flexion reproduced and maintained in the usual manner. In the third week the forearm

FIG. 2.



Fourth day of treatment.

was dressed at right angles with the arm, and at the end of the fourth week the arm was merely carried in a sling. By the end of the sixth week active extension and flexion were complete, and no trace of deformity remained.

This case has been reported in some detail, both because it represents the treatment which I think gives the best results in these cases, and because it is not often that we have the opportunity of verifying our actions by such excellent skiagrams. The advantages

which may be claimed for the position of acute flexion in such cases are many. In the first place it effects reduction and maintains it. As seen in Fig. 2, the coronoid process of the ulna rises up and locks against the lower end of the upper fragment, acting as an excellent splint, and preventing displacement of the intervening fragment. It is a position which is easy for the patient: no splint is required, and the arm is not bound to the side; hence an undershirt may be worn beneath the dressing, and can be changed from time to time without inflicting pain or producing injury to the elbow. Swelling is not an absolute contraindication to the employment of acute flexion. It is to be remembered that the greatest amount of the swelling occurs in the subcutaneous tissues, and that the brachial vessels here lie close to the joint, and are not materially compressed by the flexion of the cellular tissues; and although we know that absolute flexion of the elbow will arrest the pulsations of the radial and ulnar arteries, I think that no injury can occur so long as pulsation persists. The carrying angle is preserved by this position much more surely than by that of semiflexion or of complete extension. In either of these two latter positions any splint employed obtains its grip on the upper fragment in a very insecure fashion, since the shaft of the humerus is cylindrical, and rotation of one fragment on the other in the long axis of the humerus is not prevented. In acute flexion, however, no rotation is possible, since the ulna, which is practically the same as the lower fragment, locks upon the upper fragment. The position of the forearm—supination or pronation—is indifferent, since the ulna is not involved in these motions.

Finally ankylosis is much less apt to ensue when acute flexion has been the position employed. Children, especially boys, are so constantly employed in active motions of the arms that they are admittedly more favorable cases than are adults as regards this aspect of the case. Children by throwing balls, by climbing fences and trees, by swinging from overhead bars, and similar procedures, very soon acquire complete extension of the elbow; but if the joint were dressed in extension, or even in semiflexion, complete flexion would be acquired by no normal activities. In the adult it may at times be best to dress the elbow at right angles, because adults might not always be able to overcome acute flexion as easily as children; but I have never yet seen a case where acute flexion even in adults was attended by an unfavorable outcome in this particular. Yet if, in adults, the deformity can be overcome and reduction maintained with the elbow at right angles, I prefer to treat these patients in that position. This, however, is often impossible, as the action of the triceps in tilting the lower fragment upward and backward cannot be overcome in all patients; since even the use of an anterior angular splint and the making of extension on the forearm, as this is bandaged to the horizontal

portion of the splint, sometimes fails to maintain reduction; and the use of weight extension for fractures of the upper extremity, confining the patient to bed, is unsatisfactory in the extreme.

## SPLENIC ANÆMIA, WITH HÆMOGLOBINÆMIA AND DECREASING SPLENOMEGALY.

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OSLER<sup>1</sup> describes splenic anæmia as "a chronic affection, probably an intoxication of unknown origin, characterized by a progressive enlargement of the spleen, which cannot be correlated with any known cause, as malaria, leukæmia, syphilis, cirrhosis of the liver, etc. (primary splenomegaly); anæmia of a secondary or chlorotic type (leukopenia); a marked tendency to hemorrhage, particularly from the stomach; and in many cases a terminal stage, with cirrhosis of the liver, jaundice, and ascites (Banti's disease)."

Banti's<sup>2</sup> definition is that the disease is "an idiopathic progressive anæmia without leukæmia, accompanied by idiopathic splenic hypertrophy, sometimes also with hepatic hypertrophy."

These definitions, however, do not set the subject at rest. There is still some doubt or denial that splenic anæmia is an independent disease; but the tendency is toward admitting its individuality, yet those that admit the individuality not seldom confuse the subspecies. Osler<sup>3</sup> is of the opinion that "a special malady does exist," and he thinks that primitive splenomegaly, splenic anæmia, splenomegalic cirrhosis of the liver, or Banti's disease, are stages of one disease.

Herman Senator, at the Seventy-first annual meeting of the British Medical Association, July, 1903,<sup>4</sup> said that "splenic anæmia as a special disease cannot be distinctly differentiated from similar affections of the hæmopoietic viscera, which are called pseudo-leukæmic." This opinion has still considerable following in Germany, but is almost abandoned here. Senator is also of the opinion that the liver cirrhosis in splenic anæmia is very probably secondary, and a consequence of the splenic affection.

<sup>1</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1900, vol. cxiv.

<sup>2</sup> Dell' anemia splenica, Florence, 1882.

<sup>3</sup> Loc. cit., November, 1902.

<sup>4</sup> British Medical Journal, 1903, vol. ii. p. 573.

The chief characteristic of the malady is a marked enlargement of the spleen: only in malaria, syphilis, and leukæmia is the spleen found as large as it becomes in this disease. Leukæmia may be differentiated from splenic anæmia by a blood examination. Even in that phase of leukæmia sometimes observed, wherein the number of leukocytes diminishes to near the normal counting, the myelocytes remain. In malarial cachexia it is not uncommon to find a spleen that weighs from seven to ten pounds, and there has been a case reported where it weighed more than twenty pounds; on the other hand, a malarial spleen may atrophy. Russell<sup>1</sup> reported a case where the spleen weighed only one ounce and nineteen grains. There are many pathological characteristics in malarial spleens in chronic cases that are similar to conditions observed in the spleen of splenic anæmia, but the pigmentation of malaria is much more marked. The trabeculæ and the areas in the neighborhood of vessels are very melanotic in protracted malaria; and the plasmodia, broken down, with pigment and the remains of cells, are often found in the splenic veins. The malarial parasite commonly disappears a short time after death, and this absence, with the fact that a malarial cachexia is possible without any previous fever, might make the diagnosis somewhat obscure. The differential blood count alone between malarial cachexia and splenic anæmia shows nothing, except that the large mononuclear leukocytes will be more numerous in malaria than in splenic anæmia. It is possible also to have a coincidence of malaria and splenic anæmia—Osler reported a number of such cases—but this is a mere coincidence and nothing more.

Syphilitic gummata may make the spleen very big, especially in congenital syphilis, but the history, the irregularity of the liver, and the more moderate enlargement of the spleen would render the diagnosis clear. The amyloid spleen of syphilis, bone caries, and other diseases have characteristic accompanying symptoms.

The microscopic appearances of the blood in splenic anæmia and pernicious anæmia occasionally have resemblance, but in pernicious anæmia the spleen is either normal in size, or reduced, or only moderately enlarged; it has been found as heavy as nineteen ounces,<sup>2</sup> but this size is altogether exceptional. In 40 cases of pernicious anæmia in Osler's wards, the spleen was palpable in only 6 cases—merely felt and not at all markedly enlarged. In 12 cases of splenic anæmia collected by Rolleston, the average weight of the spleen was 61 ounces; in Bovaird's case it weighed 12½ pounds, and a weight of, at the least, 30 ounces is quite common.

In primary cirrhosis of the liver with secondary splenic enlargement, the spleen does not approach the weight found in splenic

<sup>1</sup> Malaria and Injuries of the Spleen, Calcutta, 1880.

<sup>2</sup> Hunter. *Lancet*, September 22, 1888.

anæmia. Kelynnack<sup>1</sup> found in 84 cases of cirrhosis of the liver that the spleen weighed on an average 12.93 ounces. In another series of 114 cases<sup>2</sup> the average weight was 9.8 ounces—about two ounces above the normal weight. In still another series of 47 directly fatal cases of primary cirrhosis of the liver the average weight of the spleen was 11 ounces, and in 67 cases, where death came from intercurrent causes, the weight was only 9 ounces.<sup>3</sup> There is, moreover, an explanatory history of alcoholism or syphilis in the vast majority of the cases of primary liver cirrhosis, but this etiology is absent in splenic anæmia. Specific fevers, malaria, gout, and rachitis cause cirrhosis of the liver—some certainly, others very probably. Hamilton<sup>4</sup> reported a case of cirrhosis of the liver in a child, aged six years, where there was no discoverable history of syphilis or alcoholism; and Rolleston and Haight<sup>5</sup> described a congenital case with syphilis excluded. These very exceptional cases do not materially affect the differential diagnosis.

Banti's disease, properly so called, is primitive splenomegaly with secondary hepatic cirrhosis, and this is at times deemed a disease distinct from splenic anæmia. Banti contends that the condition of the liver is a consequence of the splenic condition, not a cause.<sup>6</sup> Dock and Warthin<sup>7</sup> even hold they could demonstrate in one of their cases that the splenic hyperplasia was older than that in the liver, because in the spleen the fibrous tissue was relatively in greater abundance, more dense, more hyaline, different in reaction to Van Gieson's stain, and more atrophic in the parenchyma. Banti, Bovaird, Stengel, and Brill have undoubtedly found clinically in closely observed cases the splenomegaly to precede the enlargement of the liver.

There is, then, either a distinct disease, splenic anæmia with or without hepatic cirrhosis, or a new kind of cirrhosis of the liver, wherein the spleen is twice or thrice as large as the spleen in the known cases of primary hepatic cirrhosis and the usual etiology of this cirrhosis is missing, or another unnamed blood disease, differing in a marked degree from the anæmias and leukæmias already classified; in any case the condition should have a special name, and, for want of a better, we may call it splenic anæmia. Cabot reasonably objects to this name, but it is becoming as fixed as terms like hysteria and hydrophobia.

Banti, in all his articles on this disease, says the etiology is unknown, and the many theories offered to explain its origin are not convincing. Barr<sup>8</sup> traces the disease to a vasomotor paresis of

<sup>1</sup> Allbutt's System of Medicine, vol. iv. p. 531.

<sup>2</sup> Rolleston and Fenton. Birmingham Medical Review, October, 1896.

<sup>3</sup> Allbutt, loc. cit.

<sup>4</sup> International Clinics, series 13, vol. ii. p. 245.

<sup>5</sup> British Medical Journal, March 30, 1901.

<sup>6</sup> Dell' anemia splenica, p. 26.

<sup>7</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1904.

<sup>8</sup> Lancet, August 23, 1902.

the splanchnic area, which arises from a disease of the visceral sympathetic ganglia. The result, he says, is an engorgement of the abdominal viscera, especially the liver and the spleen, with hæmolysis as a consequence. The blood stasis leads to fibrosis and lessened functional power; it also causes the peritoneal effusion, which is, in this disease, not dependent upon portal obstruction. The same vasomotor paresis which lowers blood pressure leads to a retention of blood in the portal circulation, and consequent hemorrhage and impaired digestion. If this theory holds, the disease of the visceral sympathetic ganglia might be caused by a toxin of intestinal origin. Senator, Rolleston, and J. Mitchell Clarke are of the opinion that the toxin is of intestinal origin. That a toxin comes from the intestines is mere theory, and such intoxication has been set up as the source of as much evil as eye-strain. Sir Andrew Clark and others made it the cause of chlorosis; Bradshaw, of anæmia; Potain, of hepatic cirrhosis; Rolleston and others, of splenic anæmia; Rivière, of anæmia splenica infantum; others, of tetany, and so on almost indefinitely.

Banti thinks that the source of the splenic anæmia is the spleen itself, but the nature of this influence is unknown to him. As the normal physiology of the spleen is unsettled, it is impossible fully to determine its bearing upon any pathological condition. Bruhl<sup>1</sup> thinks that the atrophy of the spleen and its loss of function bring about alteration in the chemical constitution of the blood, and a consequent anæmia. If this were true, splenectomy should cause the symptoms of splenic anæmia, but it does not.

That splenectomy has improved or even cured cases of splenic anæmia does not necessarily prove that the spleen itself is the cause of the disease. Bottazzi<sup>2</sup> seems to find that normally the spleen, besides destroying erythrocytes takes out hæmoglobin from these corpuscles, and that removal of the spleen in dogs makes the red corpuscles less liable for a long time to lose hæmoglobin. Hunter<sup>3</sup> found that in rabbits after splenectomy toluylendiamin will cause only slight or no hæmolysis. If splenic anæmia is a chronic toxæmia, splenectomy may render the erythrocytes less liable to destruction by leaving the hæmoglobin more stable. This explanation for the effect of splenectomy is offered by Rolleston.<sup>4</sup>

Again, splenic anæmia seems not to be caused by an increase in the hæmolytic function of the spleen, because its abnormal enlargement in that malady is not a real hypertrophy, but an effect of cirrhotic atrophy; and there is not an unusual evidence of iron or pigment to show excessive destruction of erythrocytes in the spleen itself. Still, it might send out a hæmolytic enzyme to act in the general circulation—but that is a mere guess.

<sup>1</sup> Archives générales de méd., June and August, 1891.

<sup>2</sup> Archiv. ital. di biologia, 1895.

<sup>4</sup> Allbutt's System of Medicine, vol. iv. p. 523.

<sup>3</sup> Lancet, 1892, vol. ii. p. 1259.



All the positive work done toward determining the nature of splenic anæmia has been directed toward the pulling down of explanatory theories, and we know almost nothing of the fundamental causes of the disease. The origin is probably a toxin of such a nature that it is made virulent by the physiological action of the spleen itself, and the blood changes are thus effected. The splenomegaly and the hepatic condition might be explained by congestion and loss of function, if we could find the cause of such stasis; to attribute it to vasomotor paresis is sheer conjecture. There is a condition commonly classed with splenic anæmia, in which the proliferation of endothelium is so marked as to suggest a primary endothelioma of the spleen; here again we are at a loss for causes.

The principal changes in the spleen in splenic anæmia are:

1. An atrophy of the Malpighian bodies, which is caused by an *overgrowth of connective tissue about the central artery, or by an ingrowth of fibrous tissue from the periphery.*

2. A thickening of the capsule, the trabeculæ, the walls of vessels, and of the reticular lining of the spaces in the splenic pulp.

3. A proliferation of the endothelial lining of the splenic vessels and the blood spaces of the pulp. This proliferating endothelium is large, with clear cytoplasm, and the nucleus is peripherally placed. The proliferation may be absent, but often it is the most noteworthy quality of the case. Based on the supposition that the dissolution of blood corpuscles normally takes place in the spleen by means of an enzyme formed from the endothelial cells of the pulp, there is an opinion that in splenic anæmia the marked increase of endothelium is the cause of the hæmolytic in that disease. The origin of the endothelial proliferation is not known, and, as has been said, in numerous cases it is not enough in evidence to explain the conditions.

Brill, in an article entitled "Primary Splenomegaly—Gaucher Type,"<sup>1</sup> which is a report on one of four cases occurring in a single generation of one family, and presented in collaboration with Mandelbaum and Libman, holds that primary splenomegaly is a distinct disease not to be classed with splenic anæmia. In this type, he says, the liver may be enormously enlarged as the spleen is, and the proliferation of endothelium is very marked. In his case the spleen weighed eleven pounds and the liver ten pounds—the weight of the normal spleen is very variable, but it is about seven ounces; that of the normal liver is about three pounds.

In the microscopic examination of the spleen in Brill's case the usual fibrosis was found, but added thereto was an enormous proliferation of endothelium in the splenic alveoli. These cells were found also in the liver—some in the lobules, but most in the con-

<sup>1</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1905.

nective-tissue spaces. The mesenteric, bronchial, and retroperitoneal lymph nodes were practically transformed into masses of endothelium, and such cells were found in the bone-marrow. Gaucher<sup>1</sup> would have this condition considered endothelioma of the spleen.

Stengel<sup>2</sup> makes primitive splenomegaly a division of splenic anæmia, and he thinks that while it is not possible perhaps to distinguish this variety clinically, there is a sharp distinction in the pathological characteristics. In one of his cases the presence of endothelial proliferation throughout the spleen was as marked as in Brill's case, but as the patient recovered after splenectomy we do not know whether the endothelial cells had invaded other organs. He discusses the question whether this endothelial growth is a neoplasm or a hyperplasia. In some cases the predominating characteristic is a fibrous hyperplasia accompanied with endothelial proliferation, while others, like his own third case, and we may add that of Brill's, have the appearance of a tumor with active neoplastic formation, essentially and primarily involving the endothelial cells.

Brill's case certainly looks like an endothelioma with metastases; as Stengel's case recovered after splenectomy, there were probably no metastases, if it were indeed an endothelioma; and as an endothelioma is not so malignant as other tumors of the sarcomatous group, that might in part account for the lack of metastases. There probably was none, because his case closely resembles our own. In our case we found very marked endothelial proliferation in the spleen everywhere, which was practically identical with Stengel's case (on comparison with a section from his case in the possession of Dr. A. O. J. Kelly), but in our case there was no metastasis. Brill, as we said, is of the opinion that in a genuine endothelioma of the spleen the liver should be greatly enlarged; in our case the liver was atrophic; it was, therefore, either not an endothelioma, or, if it was, the hepatic enlargement is not essential to the diagnosis. Probably the same is to be said of Stengel's third case, which, as far as we know, showed no signs of extraordinary liver enlargement.

In the discussion of Stengel's paper Osler drew attention to the importance of looking in the blood in splenomegaly for the protozoon of Donovan, especially in the cases that come in from the tropics. These organisms are oval, 3 to 6 $\mu$  in diameter, each of which has two nuclei. It finally develops into an elongated pointed protozoon with a flagellum—the round and the rod-shape nuclei remain. In the early form the larger nucleus is oval and eccentrically placed, and the smaller nucleus is rod-shaped, and set perpendicularly or tangentially to the larger one. This plasmodium takes the Romanowsky stain or its modifications, and the cytoplasm then is reddish.

<sup>1</sup> Splénomégalie primitive-endothelioma primitif de la rate, 1882.

<sup>2</sup> Transactions of the Association of American Physicians, 1904, vol. xix. p. 174.

The bodies occur singly or in pairs, but they may be in groups as if they had been embedded in a macrophage. They are found free and in phagocytes in the spleen, the liver, the mesenteric glands, the bone-marrow, the kidneys and adrenals, and in intestinal, skin, and mucous ulcers, but they are not found in the peripheral blood. They cause symptoms resembling malaria, but they are not removed by quinine. They commonly reduce the number of erythrocytes to from two to three million, and bring about leukopenia. Like malaria they increase the number of large mononuclear leukocytes. In ten of Donovan's cases the average percentage of mononuclears was 21.58—they varied from 6 to 48 per cent.

Clinically, splenic anæmia occurs four times oftener in males than in females, and it is commonly a disease of adults. The condition may be roughly divided into three stages: First, asthenia and perisplenitis; second, anæmia and splenomegaly; third, cachexia. In the third stage there may be ascites. The chief symptoms in general are splenomegaly; a progressive secondary anæmia with leukopenia; absence of external glandular swelling (the abdominal glands are commonly found somewhat enlarged post-mortem); notable chronicity, and in some cases a lasting hæmatemesis.

In the early stage asthenia is the chief symptom, with some wasting of the muscles, but the fat commonly remains. There may be pallor, a pigmentation of the skin, dyspnoea, palpitation; commonly there is no anorexia. The first symptom noticed in other cases is pain in the region of the spleen. This pain is increased on pressure, it radiates toward the back, the left shoulder, and the loins, and it is likely to recur. Fever as high as 102° often accompanies the pain; and there may be nausea, vomiting, and diarrhoea. The attack resembles hepatic colic, and the colic is a stage in which the disease has progressed considerably without being recognized. The spleen will then be found enlarged and tender, and it may have irregularities on its surface, especially during the painful seizures.

Rarely there is some perisplenitis, and this may be accompanied by pleurisy at the left base. There may be respiratory trouble, irregular reflex cough, some subcrepitant rales, and a diminution of the vesicular breathing sound. The perisplenitis seems to be a mechanical effect of the splenic growth.

The anæmia begins as a simple anæmia in the slow cases. Then there is a decrease of the erythrocytes and of hæmoglobin. There may be some poikilocytosis, no considerable change in the leukocytes, or a slight increase of the multinuclear neutrophils and the blood plates.

Where there is a tendency to hemorrhage, the hæmoglobin is commonly proportionately lower than the number of red corpuscles; the multinuclears decrease, the lymphocytes remain near the normal ratio, the eosinophiles may be above the normal number, and more

or less nucleated red cells may appear, but never so many as in pernicious anæmia.

Hæmatemesis is frequently though not constantly found in splenic anæmia. It is of splenic origin rather than hepatic, and it is very lasting. Osler said, "With the exception of the chronic hemorrhagic form of peptic ulcer there is no known condition in which hæmatemesis may occur for so many years." Recurrent epistaxis and bleeding from the gums may occur, and in a few cases hemorrhages into the eye fundus have been noticed. Hæmaturia and hæmoptysis are very rare.

In general, after the spleen is enlarged, the anæmia, which may last from three to ten or more years, is a marked secondary anæmia, but it has no specific characteristics, except that ordinarily in splenic anæmia the ratio of the hæmoglobin to the number of erythrocytes is lower than in other secondary anæmias. Microcytes are frequently observed. Usually there is leukopenia, but after hemorrhage, or from some intercurrent inflammatory process, there may be some leukocytosis. No micro-organism has been found in the blood.

Commonly the enlarged spleen is smooth and it retains its customary outline; indeed, any marked deviation from the outline makes the diagnosis doubtful. It may extend in beyond the navel and down to the iliac crest. The enlargement is permanent in nearly every case. If there is a cessation of this growth, the spleen does not recede in a typical case. Strümpell reported a case where the size of the spleen diminished for a while under treatment.

The liver dulness frequently goes a half-inch or more below the normal line, and jaundice is found, though rarely. Petechiæ, especially on the legs, show in the advanced stage.

The external lymphatic glands do not swell, or at most one or two glands are merely palpable. In autopsies, however, the mesenteric glands are commonly found enlarged. Bruhl would make this condition of the external glands a differential diagnostic sign in splenic anæmia.

In the cachectic stage there may be œdema, ascites, or hydrothorax. Asthenia is progressive, and diarrhœa and hemorrhages are more frequent. There is in this stage frequently considerable fever of a hectic type, which may reach  $103^{\circ}$  or  $104^{\circ}$  in the evening. The lesions of splenic anæmia are seen only in the spleen and blood, and perhaps secondarily in the liver. Other organs are affected exceptionally and indirectly.

The disease is fatal, and the treatment that has proved of value up to the present is either splenectomy before the cachectic stage, or Talma's operation. Banti advocates splenectomy in all conditions except (1) in profound cachexia; (2) in pseudoleukæmic hypertrophy of the lymphatic glands. He thinks ascites indicates cachexia. Colzi, however, according to Banti, did a splenectomy

in a case in which there was hepatic cirrhosis with some hob-nailed growth, and the patient recovered. Jean Roger<sup>1</sup> reported two splenectomies with recovery, each done in the ascitic stage of Banti's disease. Bessel-Hagen recommends splenectomy in any stage of the disease. Schiassi<sup>2</sup> reported a case of Banti's disease in the third stage, where he fixed the spleen to the parietal peritoneum. This cured the ascites, but the anæmia persisted. Twelve to fifteen grams of fresh bone-marrow from the epiphyses, and one to three grams of hepatic extract were given to the patient, and the anæmia disappeared.

Jordan,<sup>3</sup> of Heidelberg, collected 17 splenectomies for splenic anæmia, with 14 recoveries, a mortality of 17.65 per cent. Harris and Herzog<sup>4</sup> had already collected 19 cases with 14 recoveries—a mortality of 26.32 per cent. We found 13 additional splenectomies for splenic anæmia done since 1901 (there may have been a considerable number more than that) in which there were ten recoveries and three deaths. If we add these to Harris and Herzog's list there will be 32 cases with twenty-four recoveries—a mortality of 25 per cent. Without splenectomy or Talma's operation all die; with splenectomy about 75 per cent. recover; the statistics for Talma's operation as applied to splenic anæmia are not extensive enough to warrant any conclusion.

The patient that was the source of this present article was a white boy, aged eighteen years. He had no history of syphilis, alcoholism, or malaria, and he was under observation from June 16, 1904, to the time of his death, November 30, 1904. When first seen his fat was about normal, his skin was very sallow generally, and the scleras somewhat jaundiced. Along the median line of the belly the superficial veins were varicose. The spleen was smooth, and so enlarged that it went down to the crest of the ilium, and inward to a finger's breadth beyond the navel, and its outline was normal. The liver was normal apparently. The urine was high in color, somewhat overacid, with an excess of alkaline phosphates, but otherwise it was normal.

During the preceding April he had had severe pain in the region of the spleen, with nausea and vomiting, and he had had nose-bleed "since childhood." In July, 1903, he had had remittent fever (Widal reaction negative), diarrhœa with some blood in it, bleeding from the gums and nose. Dr. Samuel Wolfe, who saw him in the Samaritan Hospital at that time, says "the spleen then extended over to the right of the umbilicus." When first seen in June, 1904, quinine and arsenic were prescribed.

Between June 17 and July 16 the spleen contracted 5 cm. in length, and the body weight increased from 98 to 112 pounds. The

<sup>1</sup> La presse médicale, No. 59, vol. x.

<sup>3</sup> Berliner klin. Woch., December 28, 1903.

<sup>2</sup> Gazz. degli ospedali, 1902, No. 69.

<sup>4</sup> Annals of Surgery, July, 1901.

spleen remained unchanged in size for some time, but toward the end of October it had contracted another 5 cm.—10 cm. in all (about 4 inches). The body weight increased, with one loss of two pounds toward the end of September, from 98 pounds on June 17 to 124 pounds on October 22; shortly after this time ascites set in.

There was no hæmatemesis during the course of the disease. The gums bled somewhat almost nightly; nose-bleeding occurred only twice after June 17. The temperature went up as high as 100° or 101° frequently, and on October 27 there was dyspnoea and a temperature of 105°. The patient had one severe attack of diarrhoea and another lighter than this.



The white space is the splenic dulness on November 5, 1904; the narrow white line is the dulness on June 16, 1904. The broad white line is the liver-dulness on November 5, 1904.

The urine showed no signs of nephritis until November 21, after the ascites had appeared. There was no albumin at any time (potassium ferrocyanide test) until after the splenectomy, when a faint cloud was precipitated twice. On November 21 a few medium-sized hyaline casts and some with leukocytes appeared. Twice these casts were so numerous as to be remarkable in the absence of albumin.

At the beginning of October the left inguinal glands, the right postcervical, and some in the anterior cervical triangle were enlarged enough to be palpable. This slight swelling disappeared from the inguinal glands before the end of the month, but one of the post-cervical glands remained palpable. The liver dulness remained

normal until the beginning of November, when it showed signs of contraction.

The skin was always very sallow. At the beginning of November petechiæ showed on the legs, and the scrotum became pigmented very darkly—like an argyria stain. On November 5th minute hemorrhagic spots were observed in both optic disks, but none elsewhere in the fundi. The retinal veins were twice the width of the arteries, which were normal.

The blood examinations were as follows:

*July 10th.* Red corpuscles, 4,350,000; hæmoglobin, 80 per cent. (three observers); color index, 1.08; some poikilocytosis; many unstained centres. At this and every succeeding blood examination the blood was searched for the malaria plasmodia, with a negative result.

*16th.* Reds, 2,450,000; whites, 14,062; hæmoglobin, 85 per cent.; color index, 1.73; the intercorpuscular spaces took the stain deeply. A new Tallqvist scale was used, but three observers agreed upon the hæmoglobin percentage.

*August 6th.* Reds, 3,000,000; whites, 14,000; hæmoglobin, 80 per cent.; color index, 1.33; the intercorpuscular spaces took the stain deeply. Two observers.

*October 15th.* Differential count (whites, 8800):

Polymorphonuclear neutrophiles.	57.5
Small lymphocytes . . . . .	28.5
Large lymphocytes . . . . .	6.5
Eosinophiles . . . . .	0.5
Myelocytes . . . . .	1.5
Basophiles . . . . .	1.5
Large mononuclears . . . . .	4.0

*November 5th.* Reds, 1,630,000; whites, 5400; hæmoglobin, 65 per cent. (a Tallqvist scale, three observers); color index, 1.99. The reds were very pale, many were broken down, and they took the stain feebly; the intercorpuscular spaces took the stain. The blood coagulated so slowly it was difficult to stop it with collodion.

*15th.* Reds, 1,930,000; whites, 2800; hæmoglobin, 75 per cent.; color index, 1.94. This count is an average of four counts, repeated to avoid possible error; and the percentage of hæmoglobin was agreed to by four observers. The interspaces stained.

*21st.* Reds, 3,130,000; whites, 8800; hæmoglobin, 65 per cent.; color index, 1.03; specific gravity, 1.050; Dare hæmoglobinometer, three observers. Interspaces stained.

*22d.* Reds, 3,090,000; whites, 3800; hæmoglobin, 77 per cent.; color index, 1.24. Interspaces stained. The blood coagulated in two and a half minutes.

*23d.* Splenectomy.

*24th.* Reds, 2,770,000; whites, 6400; hæmoglobin, 69 per cent.; color index, 1.24.

28th. Reds, 3,150,000; whites, 9600; hæmoglobin, 68 per cent.; color index, 1.07. Six normoblasts were found in four slides (not cover-glasses).

A specimen of the serum, obtained upon the day the splenectomy was performed, was sent to Dr. W. M. L. Coplin, professor of pathology in the Jefferson Medical College, and the diluted serum, free, of course, from cells, gave the characteristic narrow alpha-band between D and E, marginating D; and a wider further beta-band, also between D and E. Dr. Coplin said the serum contained hæmoglobin, and more than its color indicated.

A blood examination made on May 3, 1904, before the patient came under our observation, was: reds, 2,410,000; whites, 2659; hæmoglobin, 75 per cent.; color index, 1.55. This high color index agrees with our finding.

The necessity of splenectomy had been explained to the family of the patient early in the summer, but they would not permit the operation. When he had become ascitic and was suffering from the consequent pressure, they asked that splenectomy be done. The condition of cachexia was a strong contraindication, but the success of Roger and Colzi in three cases in a similar state, and the opinion of Bessel-Hagen, were taken as a justification for doing splenectomy as a last chance.

Dr. William J. Taylor, visiting surgeon to St. Agnes' Hospital, removed the spleen. The incision through the belly wall was made from the border of the ribs to below the crest of the ilium along the outer border of the rectus muscle, and a second incision at right angles to this from the main incision outward toward the flank. There were a few slight adhesions to the diaphragm, but much adhesion along the lower border of the spleen to the sigmoid flexure of the colon. The mesenteric attachment of the spleen was stripped, the vessels dissected loose and tied with silk. One friable vein broke, but the bleeding was easily controlled. All adhesions and attachments were ligated and cut and the spleen lifted out of the belly. It weighed 945 grams. When oozing had been stopped, a strip of iodoform gauze was passed down to the stumps of the vessels for packing and drainage. The ascitic fluid welling in the belly caused considerable delay by covering the field of operation. Dr. Taylor says that in another similar case he would drain the belly by making a small opening and turning the patient on his side before operating.

The day after the operation the patient, who had reacted well after the splenectomy, became restless, and the temperature went up to 102.3°. The next day he was stuporous, his pupils dilated, and the head was slightly retracted; three days later there was some rigidity of the muscles in general, and twitching of the left facial muscles. Injections of salt solution restored consciousness, but he relapsed into the stuporous condition. The temperature ranged



from 99.3° to 102°, and there were involuntary voidings of urine and feces. The operation wound became septic with the colon bacillus from his own handling of the dressing. He died a week after the splenectomy.

*The Autopsy.* Pathological Diagnosis: (chronic splenic tumor); atrophic hepatic cirrhosis; septic peritonitis; pancreatitis; parenchymatous nephritis; slight cardiac fibrosis; pigmentation of the skin.

The body was emaciated; the skin was very sallow; the scrotum was of a blackish hue; there were petechiæ on each patella. The cœliotomy wound was purulent.

The belly: the subcutaneous fat was absent; the bowels were very anæmic and covered with purulent and flocculent exudate, and the bottom of the pelvic cavity was filled with pus. This pus, as was learned afterward, was caused by an infection from the bacillus coli communis through the cœliotomy wound. The omentum was congested and thickened throughout, and newly adherent to the stomach and over its whole surface to the belly wall. It was friable at the gastric adhesions.

The liver was firmly adherent to the diaphragm and the transverse colon, and newly adherent to the omentum. The liver was gray, hob-nailed, dense, atrophied. It weighed 910 grams. The gall-bladder was normal.

The appendix vermiformis was bound down by old adhesions. The stomach was very anæmic, inflamed in the region of the abdominal wound, and it was newly adherent to the diaphragm and the belly wall. The pancreas was indurated and very firmly adherent to all the organs that touched it, so that it was difficult to get it out. The adrenal bodies were normal. The kidney capsules stripped with some resistance, and on section the kidneys were slightly congested. The mesenteric glands were slightly enlarged.

Nothing unusual was found in the thorax except old adhesions at the back of the left lung. The skull was not opened through lack of permission.

*Microscopic Appearances.* The spleen. There was a connective-tissue hyperplasia throughout the organ. The splenic substance was transformed by this thickening and a marked proliferation of endothelium. All the bloodvessels and sinuses had thickened walls from endothelial proliferation, and these cells were so packed into the sinuses as to fill them completely throughout the greater part of the spleen. Many of the Malpighian bodies were recognizable, but they were enlarged three or four times by endothelial proliferation, and were irregular in outline. There were giant cells with nuclei grouped centrally and peripherally, as in Stengel's third case,<sup>1</sup> but these cells were not so numerous as they were in his case. A search for tubercle bacilli was negative.

<sup>1</sup> Loc. cit.

The liver had the ordinary microscopic evidences of atrophic cirrhosis. No unusual endothelial proliferation or metastasis could be found.

The pancreas showed interstitial inflammation and a considerable atrophy of tissue. There was a slight interstitial fibrosis in the heart muscle, and considerable epithelial degeneration in the kidneys, especially in the convoluted tubules, and a moderate congestion everywhere. The adrenal bodies and the lungs were normal.

The striking characteristics of this case are: (1) the fact that the spleen shrank 10 cm. during our observation—Strumpell's is the only similar case we find; (2) there was a marked true hæmoglobinæmia throughout the last six or seven months of the patient's life. A characteristic of this disease is a low color index from a decrease in the hæmoglobin; in this case the corpuscles were laked out, but the hæmoglobin seemed to remain in the serum.

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### HYPERNEPHROMA: REPORT OF THREE CASES.

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UNTIL embryologists decide where to classify a certain new-growth found in the kidney the non-committal term hypernephroma is a happy one. Whether these tumors are to be placed with the sarcomas, carcinomas or adenomas is one of the debatable questions

and will depend upon whether one makes morphology or hystogenesis the basis of classification. There is no question regarding the malignancy of these neoplasms, metastasis taking place through the blood current. Bland Sutton says, "In a few recorded cases in which adult individuals have survived nephrectomy for sarcoma more than a year the tumor belongs to the variety which imitates the structure of the adrenal."

These growths are sufficiently rare to make the report of them interesting both from a scientific and clinical point of view.

CASE I.—Mrs. M. F., aged forty-five years, mother of twelve children, youngest two years old. Twelve years ago the patient was kicked in the left side by a cow and has had occasional attacks of pain ever since. Two years ago she noticed an enlargement and

FIG. 1.



Shows tumor resting upon kidney, the capsule having been removed. (Case I.)

for the past four months has had steady pain in the side, now has difficulty in moving bowels and troubled with frequent micturition. It was demonstrated that normal urine was being excreted by the right kidney while the left excreted about one-quarter as much as the right and contained pus and blood. Operation December 2, 1901, the patient made an uninterrupted recovery, leaving the hospital in twenty-one days. Two and a half years later there were no signs of recurrence or dissemination.

CASE II.—Mrs. S. McD., aged sixty-four years, mother of five children, appetite poor, was very much emaciated. In January, February, and March, 1903, she passed bloody urine. The first attack lasted four days, the other two not so long. All pain at this time was referred to bladder region. She recovered and felt fairly well until the following January, since which time she has

had more or less pain in the bladder. Two months ago she noticed a tumor in right side which has rapidly increased in size but is not especially sensitive. She came under observation June 29, 1904. The urine from the left kidney was normal. No urine was excreted on the right side. Operation on July 6, 1904.

CASE III.—Mrs. H. R. P., aged sixty-one years, appetite fairly good, slightly constipated, she complains of dull pain starting in right side and extending to suprapubic region. She noticed abdominal tumor four years ago. She has passed bloody urine for ten years, six months ago she passed sufficient blood to cause general weakness. The patient thinks tumor has increased fully one-half

FIG. 2.



The tumor has been cut through the centre, but is still attached to the kidney. The lighter areas show necrosis. (Case I.)

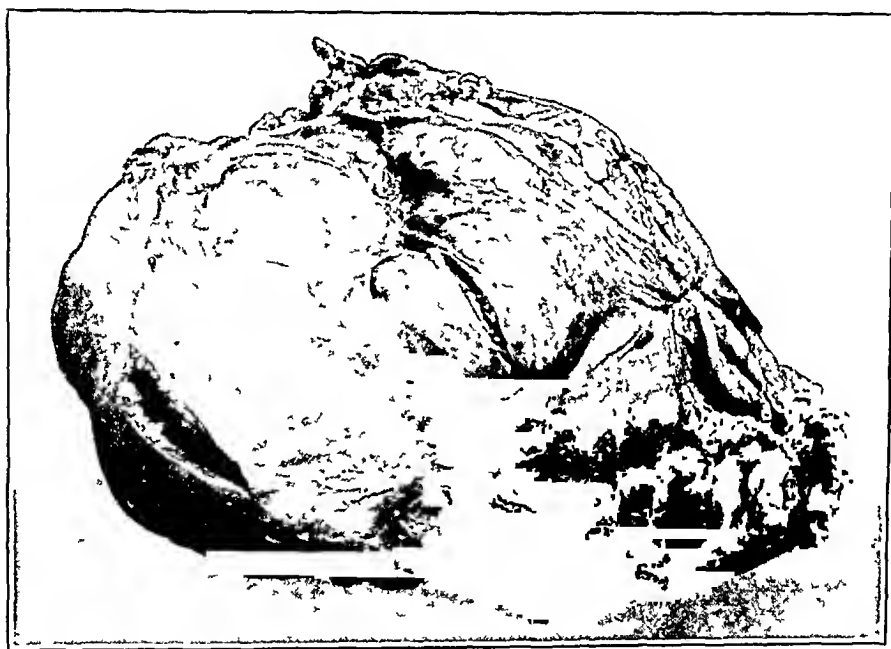
in size in last six months. The mixed specimen of urine contained pus and blood, the left kidney excreted normal urine. Some pus and blood but no urine came from the right kidney. Operation September 13, 1904.

*Gross Appearance of Kidney.* The kidney is of normal size and shape, with a smooth pale surface. The capsule not adherent except at a sulcus which marks the juncture of tumor with kidney. Cortical zone narrow and light colored, pyramids and medullary rays indistinct, fat deposits in calices. At the lower pole directly under the surface extending to but not into the pelvis is a thin-walled sac  $3\frac{1}{2}$  cm. in diameter, containing a mass of granular detritus. This area is surrounded by a hyperæmic zone.

Microscopic sections show large areas of degeneration with hemorrhages which were not discernible macroscopically. Many of the tubules contain hyaline masses and the vessels are engorged with blood. The parenchyma shows cloudy swelling and granular degeneration.

*Gross Appearance of Tumor.* Springing from the upper pole of the kidney and extending into the pelvis is a smooth growth of firm consistency measuring exclusive of kidney 10 x 24 x 28 c.m., weighing including the kidney 435 gm. It is included in the kidney capsule which can be easily stripped off except at union of kidney and growth and a small area at upper part of tumor. Median incision

FIG 3



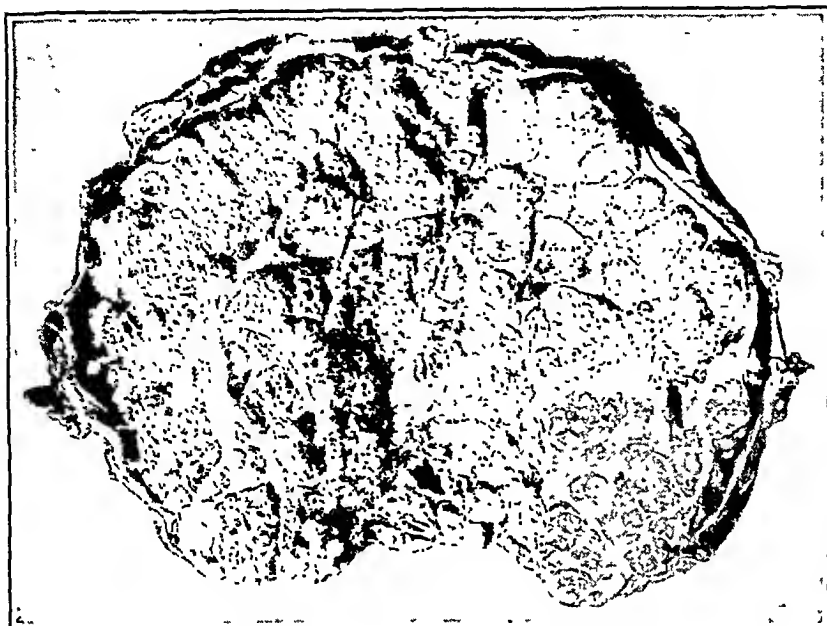
Gross appearance of tumor.

through the tumor mass reveals widespread necrosis. Two distinct areas can be seen which divide the growth about equally. A pale yellow zone of moderately firm consistency and a salmon-pink zone with whitish streaks. Thin-walled sacs similar to the one mentioned in the kidney and filled with necrotic material are found throughout the latter zone. One of these areas situated where the capsule is adherent is the only one which shows blood pigment.

*Microscopic Examination of Tumor.* On account of the extensive necrosis much difficulty was experienced in determining the true nature of the growth and then only after many sections were made from the different areas. Some sections contain considerable pigment.

Fig. 5 shows structure of adrenal cortex. At one side is seen a connective-tissue capsule. The stroma is composed of a delicate

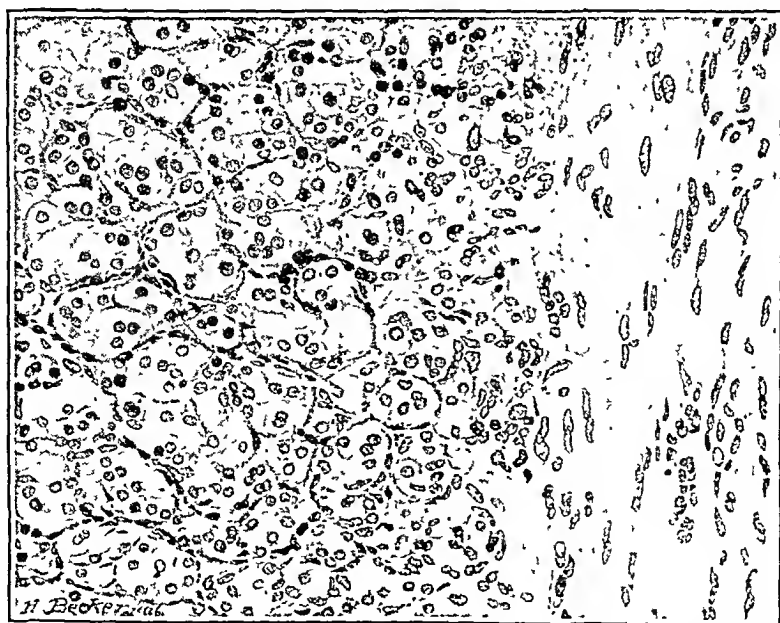
FIG. 4.



Gross appearance of growth on section.

network of capillaries in the meshes of which are round or polygonal cells with a distinct cell wall and a large amount of proto-

FIG. 5.



plasm. The nucleus is oval, large, stains well, is centrally placed and has a metachromatic nucleolus. No giant cells were noted.

Fig. 6 shows large venous sinuses with well-developed walls. The intervening broad bands of tissues are infiltrated with red blood cells and are of a complex nature, the tumor cells staining rather faintly. No similar structure was found in the growths from the other cases.

A single description will suffice for Cases II. and III., as both the gross and microscopic appearances of the neoplasms were so similar that it was impossible to differentiate them except by size. The tumor from Case II. weighed 1446 gm. and measured  $7\frac{3}{4} \times 13\frac{1}{2} \times 13\frac{1}{2}$  with a circumference of 39 cm. The growth from Case III. weighed 1616 gm. and measured  $12\frac{1}{2} \times 13\frac{1}{2} \times 16$  cm., circumference  $40\frac{1}{2}$  cm.

FIG. 6.



*Gross Appearance.* The tumors are very nodular with large engorged vessels passing in all directions over the surface. The capsule to which considerable fat is attached is firmly adherent. The cut surface is strikingly uniform. Bands of tissue of a salmon-pink color support islands of tissue of various hues depending upon the stage of degeneration. The islands near the surface are brownish-red and quite firm in consistency, while those in the centre of the growth are lighter in color and necrotic to a caseous degree. No

cysts were present and no kidney structure could be demonstrated either macroscopically or microscopically. Microscopic sections taken from all parts of the tumor exhibit the typical structure of the adrenal cortex both in their architecture and the relation of the cells to the bloodvessels, showing the same characteristics found in Section 1 taken from Case I.

The cases herein considered were operated upon by Dr. W. J. Mayo in St. Mary's Hospital, Rochester, Minn.

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## THE PROBLEM OF THE TREATMENT OF LARYNGEAL TUBERCULOSIS.<sup>1</sup>

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IN studying the indications for treatment in laryngeal tuberculosis, it will be well to briefly review some points in connection with the natural history of the disease.

**PREVALENCE.** It is probable that over one-fourth of all cases of clearly defined pulmonary tuberculosis present laryngeal lesions.

Statistics based upon (a) autopsies and upon (b) examination with the laryngoscopic mirror in the living range from 13 per cent. to 50 per cent.; the estimates are likely to be too small because of the difficulty of detecting slight lesions.<sup>2</sup>

Besides cases associated with undoubted lung disease are some in which the other foci are not so evident, perhaps not discoverable at all. Such cases seem not numerous, but this is probably only because these patients do not come under observation unless local symptoms are pronounced. It is safe to say, taking all things into consideration, that a considerable number of people suffer from laryngeal tuberculosis.

**HOW THE TUBERCLE BACILLUS REACHES THE LARYNX.** This is still somewhat a matter of conjecture. It is supposed that the greater number of laryngeal cases are due to infection from the lung carried in the sputum or through the lymph or bloodvessels, that a less number are due to infection from affected lymphatic glands, and a still smaller number arise directly from tubercle bacilli inspired into the air passages. The disease is subepithelial, always beginning, it is now believed, in connective tissue, and bacilli entering from the air passages must find entrance through the mucosa in order to reach the tissue it attacks.

<sup>1</sup> Read before the Philadelphia County Medical Society, March 8, 1905.

<sup>2</sup> There is considerable variation in statistics on the subject. Newcomb (Burnett, Ingals, and Newcomb, *Diseases of Nose, Throat, and Ear*, p. 625) states that 33 per cent. of all pulmonary cases present laryngeal deposits. Coakley (*Diseases of Nose and Throat*, p. 414) estimates the number at 20 per cent. Posey and Wright quote as follows (*Diseases of Eye, Ear, Nose, and Throat*, p. 853): Kidd, 20 per cent.; Willgk, 13 per cent.; Brompton Hospital Report, 50 per cent.



Tubercle bacilli sometimes light upon syphilitic ulcers and engraft tuberculosis upon them.

**LIFE HISTORY OF THE TUBERCLE.** Whatever the mode of entrance, the presence of tubercle bacilli leads to the formation of tubercles. The bacilli multiply and are rapidly disseminated into surrounding tissues, partly by growth, partly by lymph currents, and the invasion extends beyond the boundaries of apparent disease. As a result of the presence of bacilli, the fixed cellular elements proliferate, producing epithelioid and giant cells. An exudation of leukocytes takes place from the vessels about the infected focus, and a reticulum of connective tissue is formed from the connective-tissue matrix, being especially abundant at the margins of the growth—all of which represents nature's efforts to destroy and wall off the infection. After a time degeneration of the tubercle ensues from lack of nutrition. If the patient's health is good and the resisting forces strong, this will be in the nature of a sclerosis, a conservative healing process; if not, central caseation takes place and the tubercle disintegrates, with an extension of the tuberculous process and a setting free of bacilli.

**LOCATION OF LESION.** The vocal cords, interarytenoid fold, and arytenoids are the structures most often attacked, though any and every part of the larynx may be involved by the tuberculous process. It is likely that the sites named suffer more often because of the nature of their structure and of their lymphatic supply, and because they are most subject to motion and trauma.

**KINDS OF LESIONS.** There is a condition—a congestion of the vocal cords that sometimes appears early in pulmonary tuberculosis. It is not like the congested cords of tuberculosis of the larynx, for there is probably no implantation of tubercle bacilli; possibly it is due to action of toxins produced by the disease in the lung, acting upon vasomotor or other nerve centres. The appearance, though not pathognomonic, is at times significant of lung involvement. Treatment has no effect and the condition may persist for months, finally clearing up if the patient's health continues to improve.

In acute miliary tuberculosis, which is accompanied by miliary tuberculosis elsewhere, the laryngeal disease plays an unimportant part; the patient generally dies before the tubercles in the larynx have progressed very far.

The manifestations of laryngeal tuberculosis, other than miliary, are of four forms: 1. Superficial ulcer. 2. Infiltration of mucosa. 3. Tuberculoma. 4. Deep ulceration.

1. Superficial ulcers frequently form upon the vocal cords and other parts of the larynx, caused by the breaking down of superficial tubercles. They have little tendency toward cicatrization, and if they do heal up are apt to break down again; their surfaces often abound in bacilli, and they may remain unchanged for long periods if the general health of the patient is good.

2. Subepithelial infiltrations of the mucosa vary from mere thickenings and indurations to large club-like swellings, properly classed under tuberculomata. They cause interference with the movements of the vocal cords, either mechanically by their size or by implicating small nerve fibrils and causing perineuritis, with consequent impairment of function; hoarseness and aphonia are often produced in this way. Fungous-like thickenings of the interarytenoid folds and buddings over the commissure are very characteristic of tuberculosis.

Infiltrations of mucosa may remain stationary and harmless for months; if, however, the infiltration is accompanied by œdema, the outlook is serious, for it is often evidence of perichondritis and destruction of cartilage, ending finally in deep ulceration.

3. Tuberculomata are usually of slow growth. Beginning and remaining localized infiltrations, they form firm, tongue-like projections similar to papillomata. They usually do not ulcerate, this being probably due to the nature of their cellular construction, which is that of beginning tubercle formation. Even when they attain great size they rarely cause much obstruction to respiration.

4. Deep ulceration comes as the closing chapter in tuberculous laryngitis. It occasions pain when located where it is affected by the act of swallowing. The swollen œdematous infiltrated tissue breaks down, accompanied by involvement of cartilage. This form of disease runs a rapid and usually fatal course, but it can be said that a few cases do recover, even after considerable destruction of cartilage has taken place.

**INFLUENCES THAT AFFECT LOCAL LESION.** These are (1) favoring; (2) resisting.

1. Favoring the disease are influences that depress vitality and lower resistance: such as the presence of other diseases, and the action of toxins from pulmonary disease upon the nervous system.

2. Resisting the progress of the disease are what is known as individual immunity, inherited or acquired, and the normal resistance of healthful natural metabolism. Locally, resistance is afforded by action of cells, as is represented by phagocytosis, if it occurs, and the resistive or possibly bactericidal action of mucus and the other local glandular secretions.

**DIAGNOSIS.** A satisfactory diagnosis of the local diseases can only be made by a laryngoscopic examination. Hoarseness, aphonia, and pain on swallowing are not reliable signs, and may even be absent altogether.

**PROGNOSIS.** Clinically the progress will have to be estimated from a careful study of the patient as a whole—from data such as changes in weight, temperature, pulse, condition of the lungs and upper air tract, etc., as well as by an inspection of the larynx itself.

Enough has been given in describing the kinds of local lesions to give an idea of their probable course. Aside from the acute miliary form, the course of the laryngeal disease is usually slow;

the lesions exist harmlessly over weeks and months. In a small number, however, the progress is rapid and destructive; the appearance of the lesions and their rapid growth give warning of their serious nature.

The laryngeal disease has no direct effect upon the disease elsewhere; indirectly it may exert an unfavorable influence by affecting the general health. How far does the local disease affect the general health? When tuberculous material is inoculated into the eye of a rabbit, causing tuberculosis of the iris, it takes some weeks to develop; the disease remains localized, and, as far as can be seen, it produces no effect upon general health. Although the analogy is not perfect, it is probable that tuberculosis of the larynx, in the same way, ordinarily does not affect the general health. It is likely, in most cases, that the laryngeal disease is an index to the amount, rather than a cause, of failure of health, for the fact that the larynx is involved at all seems evidence that the resisting forces of the body have been weakened just so much. On the other hand, when the laryngeal disease causes dyspnoea, pain, or difficulty in swallowing, it cannot but exert an unfavorable effect upon the general health.

How far beyond this laryngeal tuberculosis affects the patient generally is not easily estimated. Theoretically, the local lesion may be supposed to cause a certain amount of toxæmia; it may reflexly affect the vasomotor system, etc., or reflexly affect digestion through the superior laryngeal and vagus, and it may furnish bacilli for fresh implantations, but these reasons are probably more theoretical than real.

**STATISTICS OF PROGNOSTIC SIGNIFICANCE OF LARYNGEAL LESIONS.** Robert Levy has studied the progress of general health of tuberculous patients with reference to the nature and location of the laryngeal lesions. Of 84 cases with infiltration or tuberculomata of larynx, he found that 58 got better or well (69 per cent.). Of 60 cases of deep ulceration, 23 got better (38 per cent.). Taking lesions in reference to their location, he found 103 cases of tuberculosis of the larynx without involvement of epiglottis or aryepiglottic folds; 92 got better (89 per cent.). Of 41 cases with involvement of these structures 12 improved (29 per cent.). In other words, of those with simple infiltration twice as many improved as when deep ulceration was present. Of those without involvement of epiglottis and aryepiglottic folds, three times as many improved as when these structures were involved. The cases that have come under my observation seem to bear out these proportions.

An examination of the larynx, therefore, taken in connection with what has been said, will give information about the future of the case nearly as follows:

1. Larynx free from disease; prognosis so far good.
2. Congestion of cords (vasomotor); prognosis good; examination of lung indicated.

3. Superficial ulcer, localized infiltration, or tuberculoma; chances of improvement about 69 per cent.
4. Deep ulceration; chances of improvement about 38 per cent.
5. Lesions of vocal cord, ventricular band, or interarytenoid fold; chances of improvement about 89 per cent.
6. Lesions of epiglottis or aryepiglottic fold; chances of improvement about 29 per cent.

This brief review of a somewhat complicated subject gives some idea of the problem of the treatment of laryngeal tuberculosis. In short, we have to deal with an insidious, intractable, subepithelial infection, the germs of which lie hidden in and beyond the limits of apparent disease. The local disease usually represents an extension of the disease from elsewhere, and affords evidence of the weakened condition of the resisting forces of the body. Many of the milder forms remain stationary over indefinite periods if local irritation is prevented and the general health improves. The disease probably does harm only when it causes dyspnoea, pain, or prevents the taking of food. Although ulceration, when it occurs, shows little inclination to cicatrize, it often does heal up under treatment; indeed some of the worst forms have recovered without any treatment.

TREATMENT is directed toward liquefying and removing secretions from the upper air tract, toward relieving congestion and lessening irritation, and toward destroying tubercle bacilli and the diseased area produced by them.

General treatment, too, is of great importance in all cases. Careful attention must be paid to improvement of metabolism and general health. These are attained by carefully considered forced feeding, fresh air, sunshine; by suitable climate, dwelling, clothing, etc., and by preventing fatigue.

Local measures include the use of gargles and sprays of alkaline and antiseptic liquids; such as Seiler's solution and hydrogen peroxide; of the application of astringents and alteratives, such as nitrate of silver (2 per cent.), argyrol (30 per cent.), iodoglycerin, creosote (5 gr.), menthol (5 gr.), olive oil (1 oz.), euophen in oil, etc.; of intralaryngeal injections and insufflations, and of treatment of ulcers with lactic acid, iodine-bearing powders, and formalin. Cocaine, menthol, and iodoform are employed to lessen pain.

The x-ray promises to be of use in certain cases, as illustrated in the following case. The case illustrates, also, the chronic nature of the disease, and how the treatment has to be varied.

*Case of Tuberculosis of Larynx.* J. K., aged thirty-seven years, first examined June 20, 1903; height 5 feet 6 inches; weight 122 lbs. Symptoms: cough, hoarseness, dryness of throat, aphonia at times, flushing, night-sweats, loss of weight, anorexia, tubercle bacilli in sputum; right apex infiltrated, with softening. Temperature, 99°.

Appearance of larynx June, 1903: Ulcer on left side of epiglottis; slight hyperæmia of vocal cords. Treatment; hygienic and dietetic. Iodoform and tannic acid insufflated not well borne; changed to lactic acid 50 per cent. every other day; alkaline wash.

Appearance September, 1903: General and local conditions much improved. No cough; no night-sweats; has gained ten pounds.

Appearance October, 1903: Has had severe cold. Inflamed area extending; perichondritis of upper left epiglottis; slight infiltration of interarytenoid fold. Treatment: lactic acid irritates; iodo-glycerin tried a few times. Throat was exposed to radium (18,000 bromide) over a period of six weeks without result (every other day, ten minutes increased to a half-hour).

Appearance December, 1903: When x-ray was begun, ulcer of epiglottis; tuberculoma of commissure. Other local treatment stopped.

At end of second week, inflamed area of epiglottis smaller; tuberculoma larger. Because of inflammation, x-ray was stopped for a week and then begun again (high tension; five-minute exposure over neck and lung every other day).

Appearance after eight weeks of x-ray. Ulcer almost healed; tuberculoma pale and shrunken; all signs of inflammation gone. General health fair; lung better; weight varies between 126 and 132 pounds.

Patient's lung was examined January, 1905, and old lesion could hardly be located. He works regularly and seems in perfect health. Weight, 135 pounds.

Upon the subject of *radical local measures* the profession is divided. The first, or conservative party, states that the position and construction of the larynx render usual surgical principles inapplicable; that although infiltration and tuberculomata are localized it is impossible to eradicate the disease by removing them, the bacilli being in the tissues and lymph channels beyond the region of visible disease, and besides there is a risk of breaking down barriers erected by nature and opening fresh regions to infection; that the body has other foci of the disease, the laryngeal infection being secondary and usually less important. It claims that the percentage of recoveries is greater without operation.

The second party is disposed to remove localized infiltrations with cutting forceps, etc., if the disease of the lung is slight and the general health good. Some advocate the use of the galvanocautery, and others inject guaiacol, creosote, or lactic acid into the swellings. In unfavorable cases, with rapid extension of disease, they advise incisions to relieve tension and favor the exit of necrotic tissue; growths are to be excised, deep ulcers curetted, and, if dyspnoea is distressing, tracheotomy is to be performed.

The question can only be settled by statistics covering large numbers of cases studied over a considerable period. It will be

interesting to compare results of cases untreated locally with those under conservative and with those under radical local treatment. Until such statistics are at hand, it will be safe for those not thoroughly experienced to follow Sir Felix Semon's advice: "Let infiltrations alone, as far as surgery is concerned; curette, and apply lactic acid to ulcers if single or few and involving vocal cord, ventricular band, or interarytenoid fold. Ulcers on epiglottis, aryepiglottic fold, or arytenoid are not so amenable to treatment.

In the majority of cases indications for local treatment may be met by directing the patient to spray the nose twice a day with an alkaline solution such as Seiler's, followed by an oil spray of camphor 3 gr., menthol 10 gr., and liquid albolene 1 oz. The teeth should be cleansed at the same time and a gargle used of peroxide and lime-water equal parts. Glycerite of tannic acid can be applied lightly to the lower turbinates every third day and to the rhinopharynx, and zinc sulphate 2 per cent. to the larynx. If the laryngeal mucosa is red, dry, and swollen, argyrol 25 per cent., or menthol 5 gr., creosote 5 gr., and olive oil 1 oz., can be applied, or the latter be given by intralaryngeal injection. The injections are given daily or twice a day, and produce most satisfactory results.

If ulcers form, the therapeutic technique is as follows: Apply 10 per cent. cocaine thoroughly with laryngeal cotton-tipped applicator, cleanse larynx with spray of peroxide and lime-water, and then with alkaline solution. After a lapse of five minutes apply lactic acid, beginning with 25 per cent. every other day, increasing strength and lessening interval until pure acid is used or ulcer heals. If signs of irritation appear, lactic acid is withheld for a time and menthol-creosote oil substituted. Treatment is completed by insufflating iodoform and orthoform powder. Lactic acid cauterizes the ulcerated area only, and, although painful when applied, lessens pain afterward markedly. Formalin is regarded by many as superior to lactic acid.

Perhaps it is not too much to hope that by the use of antitoxic or antituberculous serum, we may some day be able to add an artificial immunity to the immunity already possessed by the patient, and be able, by its use, to prevent tuberculosis. Studies are being made in this direction, and in some ways the outlook is very bright.

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## TUBERCULOSIS OF THE PROSTATE.

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TUBERCULOSIS of the prostate has only recently become a subject of more than passing interest. Pathologists recognized the disease long ago and knew it to be not an infrequent condition, at least as a part of a more or less generalized genitourinary infection, but no adequate recognition of its clinical importance appears in the literature before 1892, when Marwedel<sup>1</sup> described four cases from Czerney's clinic and reviewed the subject in considerable detail. The earlier urologists looked upon it as a relatively rare and unimportant disease. Sir Henry Thompson in 1873 says that "the prostate is very rarely involved in tuberculous diseases, and is never affected alone or primarily." Socin in 1875 held a similar opinion as to its rarity, though he recognized a primary form. In a recent edition of his monograph (Socin and Burckhardt, 1902) more attention is given to the clinical importance of the subject, both in its primary and secondary aspects. Von Frisch and other recent monographists also refer to it as a disease of common occurrence and bring forward its clinical importance, though most text-books dealing more generally with genitourinary surgery fail to give it adequate recognition.

The following two cases of genitourinary tuberculosis<sup>2</sup> originating in the prostate have recently been examined in the Pathological Laboratory of Rush Medical College and have seemed to me worthy of report. Finding very little bearing directly upon the subject in the American medical literature, I have deemed it worth while to review the subject at some length.

CASE I.—H. J., a Welshman, aged thirty-two years, and a salesman by occupation, was admitted to the Presbyterian Hospital, Chicago, January 20, 1903, to the service of Dr. Billings. An uncle on the paternal side died of tuberculosis; otherwise the family history is negative. He has had the usual diseases of childhood, but no serious illness since.

He has been an habitual and heavy indulger in alcoholics, especially during the last four years. Recently while receiving treatment

<sup>1</sup> An alphabetical list of authors quoted will be found at the end of this article.

<sup>2</sup> The records of these cases were put into practically the form in which they now appear by Dr. Epley, who as a student at Rush began their preparation for publication. Upon his graduation he left the city to engage in practice and the cases fell into my hands. I take this opportunity of expressing my indebtedness to Dr. Epley for the work which he had completed.

for alcoholism, he had a severe diarrhoea lasting two weeks, during which he passed a good deal of mucus accompanied by colic and tenesmus. These have entirely disappeared at the present time. He states, however, that for the last five years there have been occasional attacks of pain and diarrhoea. There is a history of two attacks of acute gonorrhoea, the last of which occurred eighteen months ago, and has continued to the present time as a slight urethral discharge, with pain on urination.

On admission the patient states that on December 22d he had a chill of moderate severity followed by a temperature of  $104^{\circ}$ , and was compelled to remain in bed. There was a severe dry cough, without expectoration, and great loss of strength. He has vomited five times in the last two weeks, and on the morning of admission he vomited a small quantity of bloody material. He complains of great weakness and dizziness upon standing or stooping over; upon exertion there is precordial pain, moderate dyspnoea, and palpitation of the heart. Urination is frequent and painful.

*On physical examination* the head and neck are found to be normal, the tongue red and raw-looking. Heart's apex in the fourth interspace in the nipple line, with the left border of dulness one-half inch to the left of this. A systolic murmur is heard in the mitral area and transmitted to the left axillary region. A few rales are heard over each lung; these appear and disappear and change place from time to time. Liver enlarged, tender, and extends three fingers' breadth below the costal margin, its edge hard and smooth. Rectal examination shows small hemorrhoids. The prostate is slightly enlarged and tender; upon massaging the gland a thin, purulent fluid escapes from the meatus, smears of which show by ordinary staining a few bacilli, numerous streptococci, and a few gonococci. The extremities are normal.

On admission the patient's temperature was  $100^{\circ}$ , pulse 112, respiration 20. There were trivial variations in these up to February 7th, when a temperature of  $104.6^{\circ}$  was registered after injecting 3 mg. of tuberculin. Subsequent to this the fever was irregular, often registering  $103^{\circ}$  and tending to remain high. On March 2d the patient had a pronounced chill, followed by a subnormal temperature, which lasted until the following afternoon, when he died.

Slight jaundice and a palpable spleen were noted on February 1st. On January 21st, the day after admission, the blood count was: erythrocytes, 2,448,000; leukocytes, 8000; hæmoglobin, 70 per cent. A month later erythrocytes and hæmoglobin were practically the same, the leukocytes having fallen to 1040. Examination of the feces, January 25th, gave a negative result. Sputum examinations on two occasions failed to show tubercle bacilli. The urine on various occasions showed a small amount of albumin and much pus. No casts were present. Search for tubercle bacilli in the sediment was made on several occasions, with negative result.



A clinical diagnosis of tuberculosis involving the lungs and genito-urinary tract was made. This was confirmed by the reaction to tuberculin, after which there was evidently rapid dissemination.

*Autopsy.* The following anatomical diagnosis was made at the post-mortem by Dr. Bassoe: Caseous tuberculosis of the prostate, bladder, right kidney, seminal vesicles, epididymes, periaortic lymph glands, and left lung; acute miliary tuberculosis of the lungs, spleen, and liver; acute splenitis; chronic parenchymatous nephritis; parenchymatous and fatty degeneration, with cirrhosis of the liver; bilateral fibrous pleuritis; fibrous perisplenitis; sclerosis of the aorta and coronary arteries; chronic gastritis; follicular duodenitis.

Only the more important findings are repeated in detail.

The left lung has a universally thickened pleura, especially marked at the apex. On section a few minute grayish nodules are found scattered throughout. At the middle of the lower lobe, near the surface, is a cavity, 1 cm. in diameter, containing a purulent material. Minute grayish nodules lie about it, and there are a few small caseous areas. The right lung contains numerous miliary and submiliary tubercles, but no caseous focus is discovered.

The right kidney contains numerous grayish necrotic areas in the medullary portion. The larger of these measure up to 3 cm. in diameter, are partially excavated, and communicate with the pelvis of the organ. The cortex represents only a few pinhead-sized nodules. The mucous membrane of the pelvis is rough, ulcerated, and studded with grayish-yellow nodules.

The left kidney contains no tubercles that are visible to the naked eye. It shows the gross changes of a chronic parenchymatous nephritis well advanced.

The urinary bladder contains a small amount of turbid urine. The mucosa is dark red, showing many ecchymotic spots. In the lower half there is a cluster of circular ulcers, varying from 2 mm. to 11 mm. in diameter, with slightly raised margins and grayish, finely nodular floors.

The prostate is converted into an aggregation of communicating cysts containing a purulent fluid. The largest of these cavities is 2 cm. in diameter. The walls are thick and fibrous and contain whitish nodules of variable size. Both seminal vesicles are enlarged and have thick walls containing small caseous nodules.

In the right epididymis is a hard nodule 1 cm. in diameter. Its cut surface is gray and exudes pus upon pressure. A very small gray nodule is found in the left epididymis. The testicles appear normal upon section.

The retroperitoneal lymphatic glands leading up from the pelvis are enlarged and contain caseous areas. The largest measures 2.5 cm. by 4 cm.

*Histological Examination.* The prostate shows only here and there a remnant of the gland tubules. Surrounding the abscess

cavities are thick masses of mature connective tissue containing caseous necrotic areas, some of which have calcified central zones. In places small masses of round-celled infiltrations are present. Giant cells are present, but are found only occasionally. The vascular walls are markedly thickened and tortuous; in places the lumen is almost obliterated. The peripheral muscle tissue is in some parts well preserved.

The walls of the seminal vesicles are thickly infiltrated with round cells, especially in the mucosa and submucosa, and contain numerous small isolated and conglomerate necrotic tubercles. The muscular layer is well preserved, though diffusely infiltrated with small round cells.

Histological evidence of tuberculosis is not found in sections of the vas deferens.

The left kidney shows only changes incident to parenchymatous nephritis, and no evidence of tuberculosis. The right kidney shows variable areas of necrosis and round cells in the neighborhood of abscess cavities. No appearance of sclerotic encapsulation or of calcification is met with.

The evidence upon which to base a conclusion that the genito-urinary tuberculosis in this case was primarily located in the prostate consists chiefly in the appearance of the lesion in that gland compared to other parts. Here we find an old infection, signified by great destruction of the gland and more by the surrounding connective-tissue increase, the thickening of the vessel walls, and the calcareous infiltration of certain necrotic areas. The disease in the right kidney is of the ascending type, with greatest involvement of the pelvis and pyramids, signifying infection from below. In hæmatogenous infection of this organ the process is first located at the bases of the pyramids and in the cortex, and, according to Weigert, tends to remain long localized. It must be said, however, that various and contradictory opinions are held concerning this fact, which will be discussed later.

CASE II.—W., a Russian, aged fifty-six years, and a laborer by occupation, was admitted to Cook County Hospital December 1, 1903, to the service of Dr. Amerson. It was impossible to obtain any history from him, except that he had been sick one and one-half years.

His skin was cold and clammy; the respirations were short, rapid, and labored. The heart was rapid, weak, and irregular, while a systolic blowing was heard about the area of the apex and was transmitted to the left axilla.

The lungs were negative. The liver was slightly enlarged, extending one finger's breadth below the costal margin. The spleen was not palpable. The abdomen was retracted. The external genitalia were normal, and the legs and feet were very œdematous.

On admission the patient's temperature was 98°. He experienced

much pain upon urination. He was very restless and slept but little. On the second day his temperature was 101°. Respirations remained high, and he coughed up much clear blood and seemed to suffer considerable pain. He died at 10 A.M., December 2d.

*Autopsy.* At the autopsy held by Dr. Le Count, the anatomical diagnosis was as follows: Tuberculosis of the prostate, seminal vesicles, and right epididymis; tuberculous peritonitis; generalized miliary tuberculosis of the lungs, pleura, kidneys, and spleen; ascites, hydropericardium, hydrothorax, and anasarca; dilatation of the mitral orifice; fibrous mural endocarditis; hypertrophy and dilatation of the heart; healed infarcts of the kidneys and spleen; cyanotic atrophy and cavernous angioma of the liver; "sago" spleen; moderate sclerosis of the coronaries.

The record of findings pertaining to our subject is as follows:

*The prostate is moderately enlarged in both its lateral lobes.* The external surface has nodular irregularities. It is the seat of a conglomerate caseous mass containing in the left lobe several abscesses of 1 mm. or 2 mm. in diameter.

The seminal vesicles are indurated and contain small caseous nodules in the walls. The right vas deferens close to the prostate is thickened and very firm. From here to the epididymis it appears to be normal. The ejaculatory duct is passable for a small probe. The right epididymis has a cyst in the globus major containing approximately half an ounce of clear, straw-colored fluid. The globus minor is one and one-half times its normal size and contains small, discrete, caseous nodules, which are softer than those in the prostate. The testicle contains no microscopic evidence of tuberculosis.

The bladder presents no gross changes.

The peritoneum, lungs, pleura, kidneys, and spleen contain miliary tubercles. No old or advanced tuberculous lesions are found in any of these organs.

Histological examination confirms the gross findings—advanced tuberculosis of the prostate, vesicles, and the epididymis and miliary tuberculosis of other organs.

The prostate shows large areas of discrete and conglomerate necrosis, with marked connective-tissue hyperplasia about them. There are numerous areas of round-celled infiltration arranged in groups. The gland tubules have largely disappeared. Those remaining show much desquamation of the epithelial lining. The vessel walls are thickened. No giant cells are found, but numerous tubercle bacilli were demonstrated in the tissue and in cover-glass preparations from contents of the seminal vesicles, the walls of which contain small caseous masses and much round-celled infiltration.

The epididymis shows only areas of round-celled infiltration and necrotic areas, with slight sclerosis, endoarteritis and periarteritis.

That the prostate in this case must have been the seat of a tuberculous process prior to its development in the epididymis and vesicles is signified by the vastly more advanced lesion, the larger areas of involvement, and the excess of surrounding sclerosis of the gland lesion. The general relation between prostatic and epididymis infection will be later discussed.

**OCCURRENCE.** That prostatic tuberculosis is not a rare disease, autopsy records amply demonstrate. Collinet found the prostate involved in 44 of 70 cases of genitourinary tuberculosis; Simmonds found it involved in 26 of 35 cases; Krzywicki in 14 out of 15 cases; Oppenheim in 18 of 25 cases; R. Koenig in 31 of 45 cases; Socin and Burckhardt in 44 out of 52 cases. Of the total of 242 cases, the prostate was found to be involved in 177, or 73 per cent. The relative uniformity of the various observations goes to prove the accuracy of the result. The prostate is involved in genitourinary tuberculosis, according to Socin and Burckhardt, with considerably greater frequency than any other single organ, except the kidney.

Opinions concerning the starting point of the disease in the genitourinary organs are various and contradictory. Autopsies are rare in the early stages, and late in the disease the process is likely to be so disseminated that it is difficult or impossible to designate the original focus. Rokitansky early stated that it begins, as a rule, in the epididymis and extends upward to the prostate, an opinion shared by Virchow and by Klebs. Cohnheim and Steinthal believe the infection always starts in the kidney and involves the genital organs secondarily. Weigert holds the opposite, believing the disease to begin in the genital organs and with relative frequency in the prostate. Simmonds found in his cases the epididymis most frequently involved; Oppenheim the seminal vesicles, and Krzywicki the prostate, and they respectively considered these the starting points of the genital infection. In all of his 14 cases Krzywicki found the oldest and most advanced lesions to be located in the prostate, and was the first to advance strongly the contention that genital infection begins there in the vast majority of cases. In 2 cases it alone showed any considerable lesion.

As it concerns the genital organs proper, Desnos believes that the prostate frequently presents the first localization of the infection. Lancereaux comes to the conclusion that it is always a descending process, and that the primary focus is to be sought for in the prostate or vesicles. From both clinical and pathologic-anatomical reasons, Monod and Terrillon believe that testicular tuberculosis is usually preceded by foci in the higher gland or vesicles. Kapsammer and Kocher express similar opinions. This view is also upheld by the investigations of R. Koenig, who asserts that the prostate plays a most important part in the development of tuberculosis of the testicles, and suggests that it may act as an intermediate station, where the bacilli develop with little or no reaction, awaiting

opportunity to progress along the vas to the testicles, and that even in apparently primary testicular tuberculosis, the prostate may first contain such undiscovered lesions.

Dimitresco says that the disease may begin in the prostate, seminal vesicles, or epididymis, the latter most frequently. Reynier takes a strong stand in favor of the epididymis, a view upheld upon clinical grounds by Senn, Murphy, and other observers.

Baumgarten attempted to solve the problem of extension in an experimental way. He injected tubercle bacilli into the urethra of rabbits and produced ulcerative urethritis, with invasion of the prostate, but no extension into either kidney or testicle, although some of the animals lived a year and a half after inoculation. Injected into the epididymis they invaded the prostate, but not the opposite testicle. He infers that dissemination does not take place in a direction opposite to the secretory flow; that the tubercle bacillus, having no power of locomotion, cannot progress against the current of a secretory fluid. From autopsy experience he believes that similar conditions obtain in man, a proposition which is disputed by F. König in discussing his paper.

Of great interest in this connection are also the experiments of Paladino-Blandini. He injected various organisms, both pathogenic and non-pathogenic, into the anterior urethra of guinea-pigs, and always found that some of them reached the epididymis after a variable period. The non-pathogenic forms disappeared again in a short time; the pathogenic kept their habitat somewhat longer, but finally disappeared, unless outside influences were brought to bear. Tubercle bacilli reached the epididymis after thirty hours in repeated experiments, and frequently also the testicle and the kidney. They did not produce specific inflammatory lesions unless trauma or circulatory disturbances were brought into play. The organisms were demonstrated both by microscopic examination and by direct inoculation experiments upon other animals.

All forms of urogenital tuberculosis are in the great majority of cases secondary to primary foci in some other part of the body, chiefly the lungs, or, as Heiberg says, the bones. Our question then concerns for the most part the starting point and mode of dissemination of a secondary tuberculous infection. It seems to be amply proven that any one of the genitourinary organs may be first involved, and that either an ascending or descending extension may take place. Of the genital organs, it seems to have been clearly demonstrated, and the opinion is largely supported, that the prostate presents the earliest localization in a large proportion of cases and plays an important part in dissemination.

From the clinical side, proof of this is scarcely possible. The prostate is deep-seated and inaccessible, while the epididymis lies freely exposed, and is hence more likely to have its pathological states discovered. Furthermore, small or even considerable lesions

in the prostate may be unaccompanied by symptoms; hence adequate investigation is often not made. From the pathological side, evidence of a convincing character points to first involvement of the prostate in many cases.

Though primary prostatic tuberculosis, in the sense that no other organ in the body presents an earlier manifestation of the disease, is an exceptional and relatively rare condition; it is, nevertheless, a well-established one, both from a clinical and pathological point of view. Socin reports 2 such cases. Möller found at autopsy miliary tubercles in the peritoneum and other parts with no advanced lesion, except that of a hazelnut-sized caseous mass in the prostate. Claude records a case in which, after death from acute colon bacillus peritonitis, no other tuberculous focus was found, even in the genito-urinary organs, aside from one in the prostate. Marwedel, Krzywicki, Comitzer, Kapsammer, and others report cases equally convincing.

**ETIOLOGY.** Tuberculosis of the prostate begins most frequently in early adult life, attaining its maximum frequency between the ages of twenty and forty years—during the period of greatest sexual activity—though no period of life is exempt. Exceptionally cases are met with in children and in old age. Marwedel observed one case in a man of sixty-three years; Hoffmann, one at sixty-eight years; and Socin, one at seventy-five years. Simmonds found three-fourths of 60 cases of genital tuberculosis between the ages of twenty and fifty years, and two cases in children of one and one-half and seven years, respectively.

As in all forms of tuberculosis, heredity plays an important part in that of the prostate. In 35 cases Desnos found tuberculosis in the antecedents of 16. Fetal implantation of the tubercle bacillus is, indeed, possible the organism awaiting an opportunity of development until some external influence exerts a harmful effect upon the prostate, making it a region of low resistance.

Similarly, in those cases developing as distinctly secondary to pulmonary or other tuberculous foci, external influences are of importance as exciting causes. Trauma, on account of the protected position of the gland, plays no important part, though several cases in the literature followed falls upon the buttocks. Those things are to be chiefly considered which tend to cause congestion and inflammation of the prostate, and most frequent among these is gonorrhœa. A large proportion of cases develop subsequent to such an infection. Englisch says that simple inflammatory processes in the tissues surrounding the prostate may play an important part. Urethral strictures, cystitis, excessive coitus, onanism, exposure to cold, infected sounds, and sound traumas are generally conceded as exciting causes. Still, a few cases develop without any such discoverable influence.

Obviously, the one etiological necessity is that the tubercle bacillus shall find its way into the gland. In what way does this take

place? Generally by direct implantation of tubercle bacilli from the blood or lymph stream, which acts as the carrier from distant parts. Jani made the interesting and important observation that tubercle bacilli are often found in the healthy prostates of those suffering from phthisis. He was able to demonstrate them in 4 out of 6 cases examined. Here they may rest until some of the influences noted above are brought into activity. Weigert had already called attention to the fact that in at least half of all pyæmic processes abscesses are to be found in the prostate. He believes, therefore, this gland is especially predisposed to the lodgement of organisms. Upon this ground Jani explains the numerous tubercle bacilli which he found in smears from prostatic fluid. In sections the organisms were found in the region of the gland tubules, between and beneath the epithelial cells, with the merest trace of tissue reaction about them.

It is also possible that bacilli may pass from the circulation through an intact kidney with the urine and be carried down to collect in the prostatic sinus, where the numerous ducts of the sieve-like floor of the urethra offer ample opportunity for lodgement and growth. That the kidney is passable by certain micro-organisms without itself becoming the seat of pathological changes has been shown by Grawitz and other observers.

Primary prostatic tuberculosis offers rather more difficulty to explanation than secondary. The blood stream is probably the chief mode of infection in these cases also. Pathological observation furnishes abundant evidence that the bacillus may pass through a mucous surface and produce no discoverable lesion. Note the frequency of infection in lymph glands draining exposed surfaces, especially the throat, lungs, and bronchi. From these glands the organism may find its way into the blood stream, without having produced any visible local lesion, and be lodged in the prostate—Weigert's "place of predilection."

Direct infection of the prostatic urethra by the use of bacillus bearing sounds or catheters is to be looked upon as a possible though certainly in this day a very rare mode of infection.

The possibility of infection through coitus has been much discussed and variously interpreted. Marwedel says it is not to be proven and that all evidence stands against it. Kapsammer is convinced that it does not occur. Excessive intercourse may indeed furnish the opportunity for latent germs to develop or for those in the blood to locate and grow, but this relation is to be sharply distinguished from a true cause—a direct infection from the tuberculous female genitalia. If infection did occur in such a way, it is reasonable to suppose that tuberculous lesions of the glans or urethra would precede the deeper localization and would be relatively much more frequent than the deeper disease.

Tschlenoff has recently investigated this subject fully. He observed a case of primary tuberculous ulceration of the penis, sup-

posedly of venereal origin. He was able to find but one other case in the literature. In neither case was the lesion proven by autopsy to be primary. He was able to collect a small number of reported cases of secondary tuberculous autoinfection of the penis, but they seem to be rare. Dobroklonsky, who is stated to have given the most attention to this subject, is only able to assert the possibility of infection by coitus.

Krecke attempted to explain the absence of peripheral lesions by the fact that the urinary stream would wash out bacilli from the urethra, but when they had once attained to the prostatic sinus conditions would be favorable to their development. If constantly washed away, how are they to reach the prostatic sinus? He compares it to the way in which tubercle bacilli reach the lung through the upper air passages; but the case is very different, for here they are carried by the air current and deposited directly upon the walls of the alveoli and smaller bronchi.

Schuchardt maintains not only that infection may occur from sexual intercourse, but that such infection is frequent, mixed with the ordinary venereal diseases. He cites several cases in support of his opinion, and suggests that the tubercle bacilli found in healthy prostates by Jani may be the result of mixed gonorrhœal-tuberculous infection. One of his cases with acute posterior urethritis developed an abscess in the prostate, the pus from which showed gonococci and tubercle bacilli. The case resulted in recovery. No sufficient evidence is given of the previous absence of tuberculosis. Both his work and his conclusions are forcibly criticised by Kraske. Cornil and Babes found tubercle bacilli and gonococci in a case presenting only the signs and symptoms of gonorrhœa. Klebs reported a case where acute miliary tuberculosis developed after gonorrhœa, suggesting a mixed infection. But none of these cases carry convincing proof of infection by coitus.

As already stated, Baumgarten produced ulcerative urethritis with extension into the prostate by injecting rabbits' urethras with tubercle bacilli, while Hanau produced only the urethritis by the same methods applied to guinea-pigs. These experiments cannot be considered analogous to coitus, since the organisms were actually projected deep into the urethra and in large numbers. On the side of result, local urethral lesions were produced, which are almost unknown in man, except as late involvements by extension from the prostate or as autoinfections.

On the other hand we must consider the experiments of Paladino-Blandini as being of great importance in this relation. While he did not produce deep lesions, he demonstrated that tubercle bacilli may reach a deep location from being planted on the mucosa near the meatus. If then there occurs at the same time some harmful influence upon the sexual glands, such as excessive or prolonged physiological congestion, old gonorrhœal infection or trauma, it



would seem to make direct infection from coitus a highly probable occurrence. This on the unproven supposition that similar conditions obtain in man.

Though infection by way of the urethra through sexual intercourse must be looked upon as a possibility, no sufficient evidence of its actual occurrence has yet been produced.

ANATOMY. As shown by the studies of Jani, in what may be called the prepathological stage of tuberculous infection of the prostate, the primary localization of tubercle bacilli in that organ is in the neighborhood of the gland tubules. Other studies of the early stages of the disease show that along the tubules first appears localized round-celled infiltration with progression to typical histological tubercles, which gradually enlarge, coalesce, and caseate. Tubules are compressed, obstructed, or dilated in different parts; the epithelium degenerates and becomes desquamated, filling the acini with granular detritus which may contain the bacilli. Caseous nodules appear in one or several places, in one or both lateral lobes, though very rarely in the middle lobe, and by a progressive involvement of tissue may come to include practically all the gland substance (Case II.). There is a great tendency to liquefaction and abscess formation, a fact often dependent upon secondary infection from bacteria inhabiting the urethra. Hence either "septic" or "cold" abscess may be present. When small, the latter may undoubtedly be absorbed with local scar formation. Calcification may take place in part (Case I.) or rarely *in toto*. Broca reports a case where almost the whole prostate was one calcareous mass. As rare conditions are to be noted cases reported by Marwedel and by Fuller, in which the whole gland was converted into a single large sequestrum.

In a few instances only has a pure miliary tuberculosis been observed in the prostate.

There is a tendency to early involvement of other parts of the genital apparatus, particularly the seminal vesicles and bladder, by the way of the mucous membranes. The former become the seat of isolated or diffuse caseous necrosis, following a round-celled infiltration and tubercle formation. Epithelium is desquamated; the cyst contents contain detritus, pus cells, and perhaps tubercle bacilli (Case II.). The bladder involvement first appears in the region of the urethral orifice and the trigone. In the early stages it is the seat of miliary tubercles, and later of more or less advanced ulcerative processes. The vas is usually involved by a tuberculous infiltration near the prostate, and if there is coexistent disease of the epididymis, suffers more or less throughout its whole extent. It may, however, remain free from discoverable lesions along most of its course, even with marked lesions in the epididymis and testicle.

Generalized miliary tuberculosis is not an infrequent ultimate result. Weichselbaum found a large vein of the plexus pudendalis

enclosed in a caseous mass by extension, with a rupture into the vein at one point as the source of such dissemination.

With the development of abscesses in the prostate come the more important complexities of the anatomical picture. While these are yet small they may break into the gland tubules and escape through the ducts into the urethra. If larger and progressive they come to the gland capsule, involve and ultimately destroy it and break into neighboring parts. The prostatic urethra is the most frequent site of such rupture; next come the rectum, the bladder, the bulbous urethra, and perineum. In a case reported by Vollimier and Le Dentu, the whole of the penis to within a centimetre of the glans was invaded by the abscess, not as a simple burrowing, however, but succeeding a tuberculous periurethritis produced by direct extension. A very rare result is rupture into the peritoneum, which was once observed by Socin.

Various and sometimes complex fistulæ are brought about by the rupture of abscesses from the prostate into the urethra, rectum, bladder, seminal vesicles or perineum, singly or in combination. Those passing between the urethra and rectum are relatively common. Toward the end the prostate may be entirely converted into a cavity communicating with the bladder and containing urine. Such conditions were observed by Marwedel, Conitzer, and Bond and Windel. The last-named case is particularly interesting from the fact that this cavity was as large as the bladder itself, with which it communicated by a small opening. Multiple fistulæ may open into the rectum or on the perineum.

In the early stages the volume of the prostate may not be much altered. As the disease becomes more advanced moderate enlargement is usually found, and a degree of nodular irregularity of the surface. Sometimes advanced caseation or abscess formation cause great increase in size. Reclus records a prostate measuring 64 mm. across, Lancereaux one five times the normal dimensions and Bacaloglu one three times the normal; but the rule is to have only moderate enlargement. Not infrequently, by reason of emptied abscesses, there may be actual decrease in the size of the gland.

**SYMPTOMS AND DIAGNOSIS.** If a tuberculous focus is situated deeply within the substance of the prostate, it may remain long without symptoms. Even up to the time of death may this be true. In Möller's case, in spite of a large caseous nodule in the gland, there was absolutely no history of urinary or genital trouble and a perfectly normal urine. Nor in those cases with extension to surrounding parts is the symptomatology of such a definite form as to make diagnosis always possible. Marwedel expresses the belief that more than a third of the cases run a symptomless course and that in many more the diagnosis is never made. Careful physical and bacteriological examination would no doubt do much to clear up a large proportion of these cases with slight symptoms,

I have recently observed a case of advanced disease in the prostate and one seminal vesicle, associated with tuberculosis of the epididymis, which gave absolutely no clinical symptoms. Rectal palpation left no doubt of the diagnosis.

Subjective symptoms usually develop sooner or later, often quite suddenly as the result of abuse, exposure or venereal infection, and are frequently of a most marked and troublesome character.

The most constant of these are disturbances of urination, at first slight, growing gradually in severity. There is frequency, which is greater by day than by night, pain or burning in the perineum and penis, posturination tenesmus and a feeling as if the bladder had not been fully emptied. The urine flows slowly from partial obstruction due to swelling of the gland. The symptoms often resemble closely those of the ordinary form of cystitis colli or catarrhal prostatitis with irritable bladder. Caspar makes the significant remark that the distinguishing feature between simple and tuberculous infection lies in the response to treatment. What relieves the simple forms only makes tuberculous worse. At times a constant call to empty the bladder and pain rob the patient of sleep and make him miserable indeed. Imperious call to urinate, with sharp pains radiating into the glans, usually signify extension to the bladder, and may be of such a character as to strongly suggest stone.

Acute retention may develop at any time from swelling of the prostate, or permanent obstruction render catheterization necessary for long periods. With advancing destruction the sphincters may be destroyed and permanent incontinence develop. Where there is a large abscess cavity communicating with the urethra, post-urination dribbling is likely to be present. Pressure upon the perineum may express the residue, as in one of Kapsammer's cases.

Chronic constipation is usually present, and pain in the rectum not infrequently occurs at stool. This may be slight or severe. Late in the disease fistulous tracts leading to the rectum or the perineum result in discharges of urine and pus by these routes.

Quite apart from urination and defecation, there is often a feeling of indefinite discomfort, pressure or actual pain in the perineum and rectum, which is increased by motion, sitting, or local pressure. It may be of great severity and long duration. Von Frisch tells of a patient who could neither sit nor lie down for weeks, using an apparatus for suspension in a standing posture, and where heroic doses of morphia failed to give relief; and of another who suffered greatly and constantly for some days after a rectal examination. Such severe pain is observed only when abscess is present.

To hæmaturia has been ascribed a more or less important place in the symptomatology of prostatic tuberculosis by most observers. Guyon, Socin and others say that it has no essential significance. Certainly it is rare as an initial symptom, though this has been observed by Gaudier and others. As a rule only a few drops of

blood are seen at the beginning or end of urination; more rarely it is discharged by the urethra between times. Exceptionally it may be discharged with the urine in large amounts. Clots in the bladder led to acute retention in one of Marwedel's cases where the bleeding was severe and prolonged. Reliquet records a case of veritable urethrorrhagia where pure blood followed urination. In whatever form hæmaturia occurs it signifies ulcerative processes communicating with the urethra or in the bladder. If continuing between periods of micturition it comes from ulcers in the deep urethra.

Frequent seminal emissions are observed in not a few cases. They are sometimes painful. There may be a few drops of blood tinging the discharge, and this may come from either the vesicle proper or be mixed with the semen in its passage through the prostatic urethra. Sexual power is generally well preserved, even when abscesses and fistulæ are present. In one of Kapsammer's cases there was a prostatic abscess with openings both to the rectum and the perineum and still no interference with ejaculation, urination or defecation. Seminal discharges may reach the rectum or bladder through fistulous tracts, events which are recorded by several observers, and in spite of this coitus may be carried out with normal sensation.

Urethral discharge is often present. This is sometimes a thin mucous substance containing granular detritus and a few pus cells, which Englisch has shown may occur in tuberculous individuals as a result of degenerative changes in the urethral mucosa without local infection. At other times it is purulent or composed of broken-down caseous material and signifies an abscess cavity communicating with the urethra or ulceration in the urethra itself. There may be a constant slight flow, though the rule is to have a few drops appear at the meatus at the end of micturition, after defecation or as a result of pressure upon the prostate from the rectum. Should a discharge appear after a suspicious coitus, it may simulate a gonorrhœal infection and be so interpreted by the patient. Marwedel and Kapsammer each report a case where such discharge, appearing fourteen days after exposure, marked the first symptoms of the disease. The physical character of the pus and the absence of the gonococcus are the distinguishing characteristics and a diagnosis is rendered certain by the finding of the tubercle bacillus, which systematic examination of the expressed prostatic fluid rarely fails to do.

The diagnosis of tuberculosis of the prostate usually cannot be made from symptoms alone. To a careful review of such as are recorded above, with the general symptoms of tuberculous infection, must be added a painstaking physical examination, which will rarely leave the clinician in doubt except in incipient primary cases. When the disease is well advanced, when there is extension to other parts, and especially when fistulæ are present, its recognition

becomes simple enough unless old uncured venereal infections complicate the local condition.

Passing of the catheter or sound reveals painful obstruction in the prostatic urethra. In the early stages this is due to swelling of the gland, later to ulcerative processes. When the latter become severe it may be impossible to enter the bladder with an instrument of ordinary form on account of the tip engaging in pockets. A woven catheter of the Mercier type may pass readily enough, though with instruments of whatever form it may be impossible to free the tip from ulcer margins or cavities into which it finds its way. Where the prostate is converted into a cyst or a series of large communicating cysts it is rarely possible to complete the introduction and false passages are readily made through the friable tissue. Pain is often severe. In a case I have recently examined it was practically impossible to introduce a small soft-rubber catheter on this account, even after 4 per cent. cocainization.

The rectal examination is one of the most important procedures. Conitzer quotes Guyon as saying: "It is, so to speak, quite as necessary to frequently palpate the prostate in those who suffer from diseases of the urinary apparatus as to examine the heart in rheumatism." The gland is, as a rule, moderately enlarged, the lobes of unequal size and the surface marked by nodular irregularities, "feeling as if grains of lead were covered with an elastic parenchyma." (Forgue). Diffuse tenderness may be present, but more important are localized tender spots. When abscess forms tender fluctuating projections may be felt; when empty, they leave pit-like depressions. Tender swellings on the prostate, developing chronically and without discoverable cause of a venereal nature, are nearly always tuberculous. The finding of fistulous openings into the rectum is frequent in late cases. They may usually be felt by reason of slightly indurated margins and fast adhesions between the rectum and prostate about their openings. If brought into view by the proctoscope they may sometimes be seen to discharge urine. When the seminal vesicles are involved they are enlarged, tender and resistant, "as if filled out with wax." (Marwedel.)

The condition of the urine will vary greatly according to whether or not and to what extent the bladder is involved. It may remain entirely normal, as in Möller's case. The reaction remains acid, even when much pus is present, and a few blood cells are frequently found in the sediment. Acid urine containing pus from the bladder is to a certain extent characteristic, the acidity often persisting in spite of catheter or other secondary infection. Tubercle bacilli in the urine are relative to the destructiveness of the process. If they are not found it is no argument against an otherwise confirmed diagnosis.

When it is possible to render the bladder contents clear enough for a cystoscopic examination, this may be of great value. It not

only tells the condition of the bladder but the stage of advance of the disease, miliary tubercles representing an early, ulceration a later stage. It also enables one to recognize extension into the upper urinary passages. The examination is likely to be very painful. For this reason von Frisch discards it entirely for a majority of cases. The endoscope shows a congested prostatic urethra, ulcers, swollen calliculus seminalis, or fistulous openings on the urethral floor.

In the early stages, where the prostate is alone or chiefly involved, systematic expression of the prostatic fluid and bacteriological examination should always be resorted to in the hope of confirming a suspected diagnosis by the finding of tubercle bacilli.

**COURSE AND PROGNOSIS.** Tuberculosis of the prostate is always to be looked upon as a grave disease. The course will be rapid or slow according to whether the general health, strength and habits of the patient are good and whether the disease is local or only a part of a diffuse infection. A limited involvement in a strong individual offers the best prognosis. The general tendency is to progressive involvement of other parts of the genitourinary apparatus, abscess and fistula formation, and death from sepsis, uræmia or generalized tuberculosis.

The disease may, however, remain long localized and latent. Mitscherlich cites a case that became active as the result of a gonorrhœal infection after sixteen years' standing. A case cited by Berand and Robin remained stationary for six years, and other observers record cases which remain for a long time quiescent and benign.

Spontaneous healing occurs in a minority of cases. Small caseous areas may suppurate and discharge through the urethra and heal by cicatrization; they may become encapsulated and latent or they may undergo calcification and encapsulation. Von Frisch states that he has seen two cases recover even after the bladder had become involved. Even when fistula formation and extensive complications are present, if no extension to the kidney has occurred, healing may take place spontaneously or as the result of operative intervention. Rectal fistulæ, and especially rectovesicular fistulæ, are likely to give rise to septic infection. They are not, however, to be looked upon as hopeless.

Supposed healing is to be accepted with reserve; recurrence is likely to occur. Klebs makes the statement that the gland once infected very seldom becomes entirely free. The earlier the diagnosis is made and the more strictly localized the process, the better are the results of treatment, hence the better prognosis.

**TREATMENT.** Tuberculosis of the prostate is amenable to surgical treatment in a certain small proportion of cases. Obviously it is only applicable when the disease is localized and limited to the genital apparatus, when tuberculosis of the lungs or other parts of the body is absent or in a latent state, and when the general condi-

tion of the patient is such as not to contraindicate operative procedures. Tuberculous abscess in the prostate should always be opened through the perineum in time at least to prevent its rupture into the rectum, which endangers the genital tract to secondary infection from fecal matter.

Marwedel says that abscess and fistula formation give the first indication for surgical interference, a course which seems to have been adhered to in the great majority of instances. He suggests, however, that it is not apparent why, when one has the opportunity to diagnose a prostatic tuberculosis early, when there is no general genitourinary or serious pulmonary tuberculosis, he should not directly attack the focus and attempt to cure the disease by removing it. In his recent work Socin expresses himself rather more strongly upon this point and advises surgical removal whenever the disease is limited and the patient's general condition is good, exactly as one would proceed in the case of tuberculous lymph nodes. Sarda, Fourgue and a few others express themselves in a manner somewhat similar, but generally advise great caution in the selection of cases for operation unless this is forcibly indicated by abscess and fistula or distressing symptoms.

Bryson discards surgery altogether except as a palliative measure in the late stages, for the relief of pain. In a few cases where the disease is well advanced, it seems as if operative interference had sometimes caused a more rapid dissemination than might otherwise have been expected. This is probably dependent more upon general than upon local conditions. Marwedel calls attention to cases in old men or in those already wasted by the disease and advises great caution in the use of the curette upon such people, even when symptoms calling for relief are of a severe sort. Young has recently reviewed the subject of operation from the standpoint of the seminal vesicles. From the good effect upon the higher process shown by removing an involved testicle, he is inclined to abstain from going directly into the vesicle and to rely first, at least, upon the minor operation. He expresses grave doubt as to the advisability of directly attacking the vesicles under any circumstances.

The logic of surgery would seem to lead to the conclusion of operation when the disease is sufficiently limited and seems to offer a fair prospect of radical removal. Recent improvements in the technique of prostatic surgery and its brilliant results also argue to this end. The number of operated cases on record is not yet large. Though operation as a rule has been undertaken relatively late in the disease, after the development of abscess and fistula, the results have been generally excellent. Cures have not been obtained in all cases, though a fair proportion have had that fortunate outcome, and those succumbing ultimately to the infection have nearly always received a great measure of relief from distressing subjective symptoms. If operation is to be ultimately necessary to afford such relief, it would

better be undertaken while the patient's general strength lends him a good degree of recuperative power and offers hope of cure.

Marwedel, Dittel, Sarda, Gaudier, Socin and others report cases of perfect cure. In some of the cases the disease was far advanced and the operation extensive. Socin removed not only the diseased prostatic tissue, but the seminal vesicles, part of the urethral floor and one testicle as well. Recovery is often rather prolonged and secondary operation is sometimes necessary to secure closure of troublesome fistulæ. Dittel, however, had a good recovery in one case after three weeks, without fistula or subjective symptoms remaining.

It is generally agreed that the best method of reaching the prostate for the removal of tuberculous foci is through a transverse, curved perineal incision. Operations for the opening of abscess have been carried out by both rectal and urethral routes, but these have been long since entirely abandoned. The perineal route brings the gland into view, can be rendered aseptic and is the most favorable place for fistula should this remain. When fistulæ are already present they should be slit up, scraped out with a sharp curette or excised, and followed to the prostate. Tuberculous foci in the gland are removed by the sharp spoon, the wound either packed with iodoform gauze and left open or sutured with a small gauze drain. Fistulæ leading to the rectum are opened, with division of the sphincter muscles if necessary. It is important to remove all that is possible of the tuberculous tissue. Should the urethra be opened, it should be sutured if possible. Socin and Marwedel both saw perfect recovery after such an accident, though temporary fistulæ resulted.

When bladder symptoms are severe, suprapubic cystotomy is advisable in the opinions of Mayer and Hänel, Conitzer, and Socin, and should accompany operative procedures attacking the prostate through the perineum.

Desnos exposed the prostate by a perineal incision and injected a solution of chloride of zinc into the parenchyma of the tuberculous gland and obtained sclerotic atrophy in from four to six weeks. His report was made too early, however, to be able to judge with accuracy of the ultimate results of this treatment. Parenchymatous injections of iodoform emulsion have been recommended, but the method has received very little support. Sarda and others condemn all parenchymatous injections on account of the possibility of serious accidents.

Various forms of local treatment other than operative have been tried with variable success. Lane claims to have cured a case after repeated operation had failed to give relief, by injecting an emulsion of sulphur in glycerin into a complex system of fistulous tracts, one of which opened into the rectum.

† Berkley Hill is a warm exponent of injections of iodoform emul-



sion into the prostatic urethra and bladder, advising previous cocainization or even general anæsthesia if pain is severe. Most other observers see no benefit from its use. Merwedel prefers a 2 per cent. solution of balsam of Peru, from which he saw good results. The best results of local treatment seem to have come from corrosive sublimate in solutions of 1:6000 to 1:2000, used as an instillation or irrigation. Silver nitrate is invariably harmful. In the beginning of the disease Marwedel observed good effects from cold applied per rectum.

Whatever form of local treatment requiring instrumentation applied through the urethra is capable of doing harm and is to be used with great care and foresight and graded to the patient's tolerance. Thompson long ago called attention to this, advising the avoidance of the catheter and all irritants. Desnos discards such forms of local treatment entirely. So long as the disease produces only the symptoms of a local catarrh, it should be treated by general measures only.

The general treatment is that of tuberculosis in other parts of the body: good diet, out-door life and whatever tends to improve the general health of the patient. Guaiacol, creosote carbonate and such things may be useful.

In a certain sense we may speak of a real prophylaxis against genital tuberculosis. Any tuberculous individual who is likely to be exposed to a gonorrhœal infection should be warned against the excess of danger that lies in this disease by reason of his condition. If such venereal infection occurs it should be treated with the utmost care and the patient put to bed in the mean time. He should be warned also against the possible results of sexual excesses. If a genital localization of his tuberculous infection has taken place, he should be advised to secure the greatest possible physiological and physical rest for his genitourinary system, as he would for any other system involved in a like infection.

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## A RESUME OF THE ISSUES CONCERNED IN THE DIAGNOSIS AND TREATMENT OF RENAL TUBERCULOSIS.\*

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To what extent renal tuberculosis has risen from obscurity may be judged from what follows. In the period of 1867 to 1895 at von Bergmann's clinic, of 55 cases operated upon for kidney diseases, as reported by Lotheisen,<sup>1</sup> but 2 cases of renal tuberculosis were encountered. In 1902 von Schmieden<sup>2</sup> collected 2100 cases of renal disease, representing 201 nephrectomies for tuberculosis, among which were 22 of Schede's own cases operated in the interval of 1886 to 1892. This great disparity in the number of the cases of the two operators is at first accounted for by the recognition of the bacillus tuberculosis, and eventually by a more liberal use of the cystoscope in aiding the early diagnosis of this affection.

The most commonly encountered subjective clinical symptoms of renal tuberculosis are *pyuria*, *polyuria*, *pain*, and *hæmaturia*, together with some slight constitutional disturbance. A moment's consideration shows that this symptom-complex is peculiar to other diseased organs of the genitourinary tract, and yet there is something distinctive about each symptom that attracts attention to the possible existence of tuberculosis. First and foremost, it is an axiom that painless pyuria in adults between twenty and forty, which is associated with symptoms of bladder irritability, and which does not yield to ordinary treatment, is, in all likelihood, tuberculosis of the bladder dependent upon renal lesions; and if, furthermore,

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the urine reacts acid, doubt gives way to strong suspicion as to the tuberculous nature of the disease. The urine so highly acid may be faintly cloudy (smoky) at first; and the great frequency of micturition (pollakiuria) in the beginning of the disease, due merely to polyuria, and finally the finding of the tubercle bacilli in the urine place the hall-mark on this affection.

Aside from the pollakiuria due to polyuria we have an increased frequency of micturition associated with tenesmus, the so-called "*cystite doloieuse* of Guyon," dependent on complicating lesions of the bladder, subsequently to be referred to.

Some stress has been laid upon the absence or relative low percentage of albumin in the urine as indicative of pyelitis; but if there is a concomitant nephritis of the afflicted or opposite kidney, the percentage of albumin will none the less be out of proportion to the pus elements present.

The repeated search for tubercle bacilli, even according to approved laboratory methods, is successful in a small percentage of instances. As accessories toward establishing the presence of the bacillus tuberculosis, the use of tuberculin (Koch) and animal inoculation are very often useful, and Fenwick even cites cases cured therewith. It should, however, be borne in mind that a marked reaction after the use of tuberculin and appearance of tubercle bacilli in numbers, when these were absent before in repeated examinations of the urine, may likewise denote the breaking down of a tubercular focus elsewhere in the system and the elimination of the tubercle bacilli by the kidneys. To guard against such an error, a guinea-pig previously injected with tuberculin and found to be free from tuberculosis, is to have injected into the peritoneal cavity 10 c.c. of the suspected urine. After the lapse of six weeks, if the animal does not react or succumb, it is killed with chloroform and the findings noted.

It is possible for *marked* renal tuberculosis to run an absolutely painless course; on the other hand, the pains may be as severe as in renal colic. Such "renal crises," or pseudorenal colic, have been variously attributed to congestions of the kidney, or blocking of the ureter with thickened, cheesy masses, and consequent retention of urine in the pelvis of the kidney.

The hæmaturia may mask the pyuria or be the first foreboding of renal tuberculosis, and yet may be so slight as to be barely perceptible in the cystoscopic examination. The occurrence of the hæmaturia is spontaneous and very whimsical, slight in amount, and appears even while at rest.

Added to all of these symptoms there are constitutional manifestations of weakness and loss of flesh and strength.

With such data in our possession the steps necessary to locate which kidney is the offending organ and the status of the other organ are a careful examination of the bladder and a study of the

ureteral orifices and the escape of urine, with, eventually, catheterization of one or both ureters.

To avoid any additional infection much care should be observed to carry out the cystoscopy with great cleanliness and exquisite delicacy of manipulation, in a bladder irritable from disease and whose capacity is, in consequence, much diminished.

The ureters and trigone are the centre of interest. We are told on the authority of Drs. Casper,<sup>3</sup> Willy Meyer,<sup>4</sup> and E. H. Fenwick,<sup>5</sup> that a ureter which is enlarged, angry red in its appearance, with injection of bloodvessels leading up to it, and numerous hemorrhages in the mucous membrane and ulcers thereabout with attached particles of mucus, presents unmistakable evidence of tuberculosis of the kidney of that side. Tubercles of the bladder wall are more rarely encountered.

Schede<sup>6</sup> has strengthened the chain of evidence when such changes of the ureteric meatus are present by the report of a case in which the kidney on inspection showed the evidence of healed tuberculosis characterized by small kidney, adherent capsule, adhesions to perirenal fat, and a cicatrix in one of the papillæ. Dr. Willy Meyer<sup>7</sup> has even drawn on the picture presented in the cystoscopic examination of the ureter, to prove the existence of an ascending or descending tuberculosis—viz., that in the descending form the mouth of the corresponding ureter is ulcerated, while in the ascending form it is comparatively healthy. If there surely be tuberculosis of the urinary or genitourinary system, and both ureteral mouths are not affected, but urinary analysis points to renal affection (catheterization of the ureters), the case is one of ascending tuberculosis. Finally, E. Hurry Fenwick has presented fifty cases proven by pathological findings, that such a dilated, very patulous, and vascular ureteral orifice, not necessarily ulcerated, is identical with a tuberculous kidney. This pathognomonic condition of the ureter he has aptly titled the "golf-holed ureter." For him, the finding of tubercle bacilli in the mixed urine and the presence of a golf-holed ureter, with cloudy urine or blood escaping, make catheterization of the sick kidney superfluous.

Ureteral catheterization in the light of these facts is not so necessary to establish the existence of a diseased kidney as it is to prove the presence of a proper sufficiency in the function of the opposite kidney. By the injection of 4 c.c. of a freshly prepared 4 per cent. solution of Grüber's indigo-carmin the location of the ureteral orifices can be made out and the existence of two independently acting kidneys rendered certain. But to estimate the character of renal secretion the urine from each kidney must be separately withdrawn by ureteral catheterization.

Renal tuberculosis is more common in the female than the male, and most frequently encountered between twenty and forty. Exceptionally it is due to an *ascending* affection.

- In a great number of instances renal tuberculosis is first brought to our notice by subjective symptoms of pollakiuria, or pus and blood in the urine. At this stage *naught but surgical relief* can be of avail, and provided the sister-kidney is functioning sufficiently, nephrectomy and not nephrotomy should be the operation of choice.

To warrant this it is advised to estimate the molecular concentration of the secretion of the assumed healthy kidney expressed in terms of the freezing point, or to determine the capacity of the urine for conducting currents of electricity. Koranyi, who formulated the conditions under which cryoscopy may be applied to urine as an index of renal sufficiency, demands that cognizance be taken of the quantity of *ingested fluids* and also the *quantity of carbohydrates* to ensure accuracy in the reading of the freezing point of urine.

Ureteral catheterization, devised by Nitze, received its greatest development in the hands of Casper, Albarran, Fenwick, Kelly, Willy Meyer, and Tilden Brown, and urines separately examined gave a clew as to the differences in the urine of the diseased and assumed healthy kidney; and yet we see each of these operators practising ureteral catheterization, having learned that the remaining kidney secretes a urine that is pathological, none the less advocate the removal of the tuberculous kidney on the ground that the sister-organ will regain its proper function and eventually act vicariously for the removed kidney. The following exceptions to such a course manifested themselves: Anuria developed, showing that either the remaining kidney was not capable of acting vicariously or that it too was the seat of tuberculous or other inflammatory disease, or that the diseased kidney nevertheless shared with its sister-organ the sufficient elimination of the tissue waste.

To obviate such occurrences where doubt was entertained, Koenig, Israel, Küster, Newman, Morris, and Rövsing advocated exposure of the opposite kidney only when it was decided to remove the diseased kidney. Hence the question must arise: Is there any contraindication for the operation upon a tuberculous kidney?

Until ureteral catheterization came into vogue, we formulated our indications for nephrotomy or nephrectomy mainly on the basis of the cystoscopic appearance of the ureteral orifices, assuming always that where two functioning ureters were present, one appearing healthy and one diseased, the risk of a successful operation was justified.

Koenig, Küster, Lange, Brown, Rövsing, Israel, and Senn see no reason why a totally diseased kidney should not be removed even if the opposite kidney is partially diseased, and report successful cases. Lange<sup>8</sup> even reports a case remarkably benefited who also had an involvement of the genital tract. Kümme<sup>9</sup> has warmly championed the cryoscopy of the blood, and Casper<sup>10</sup> that of the urine and blood, as furnishing the crucial signs for or against nephrectomy, and they point with much *éclat* to their lowered mortality

incident to the use of cryoscopy in singling out cases for nephrectomy.

Some exceptional cases of hæmaturia and sepsis will always justify the risk of the removal of the diseased kidney in the face of all odds of the opposite kidney.

To reconcile these conflicting opinions, a study of the statistics of operations of various epochs may be of service. Thus, v. Schmieden (*loc. cit.*) collected 201 cases up to 1902, the greater number of which were diagnosticated without the aid of cystoscope, and obtained a mortality of 29 per cent., which corresponds with a like mortality of 29 per cent. in 136 cases reported by Palet.<sup>11</sup> Morris,<sup>12</sup> who denies himself the use of ureteral catheterization, reports 18 cases with a mortality of 27 per cent, which is again exceeded by Koenig, who takes the same stand and also reports 18 cases (1900) with a mortality of 33 per cent. Contrast these figures with the advocates of ureteral catheterization:

Taffier (14), 1898 . . . . .	9 cases,	No deaths.
Tilden Brown (15) . . . . .	18 "	7 per cent.
Albarran (16), 1896 . . . . .	.....	12 "
Bangs (17) . . . . .	135 cases (collected).	5 "
Küster (18) . . . . .	17 "	No deaths.

This lowering in the death rate is certainly due to a more accurate analysis of the urines separately obtained from each kidney by ureteral catheterization.

Now, Casper (*loc. cit.*) and Kümmel (*loc. cit.*) would have us believe that their further reduction of the mortality is due to the still greater precision in the methods for determining operative intervention gained from cryoscopic findings; and yet their mortality is 14.3 per cent. and 10 per cent., respectively, two figures that are surpassed on the one hand by Israel, who in 1896 had but 12 per cent. opposing ureteral catheterization at that time, and on the other by Tilden Brown, whose mortality with ureteral catheterization was 7 per cent. This last mortality figure agrees fairly closely with that of Rövsiing,<sup>19</sup> who reports 86 cases of nephrectomy with a mortality of 8.1 per cent., performed regardless of cryoscopy, though often availing himself of exposure of both kidneys, notwithstanding the accurate urinalysis of the separate urines obtained by ureteral catheterization.

From this we must conclude that a careful study of urine analysis of each kidney is up to the present our best guide, and when doubt exists beyond this we may, in the light of the experiences of Rövsiing and Edebohls, explore with impunity the associate kidney, which will obviate errors due to anomalous conditions of the ureters.

Cryoscopy, to be of service, must be performed several days in succession, for the molecular concentration of urine varies at different hours of the same day, and is influenced by systemic diseases. To illustrate how elusive this method is, Koranyi himself has

reported a case where the freezing point of blood was normal, in spite of the existence of pyonephrosis of both kidneys. Only when a marked diminution of urea might contraindicate a nephrectomy should it be correlated with the freezing point of blood before the final negative decision.

The value of x-rays in locating renal tuberculosis is yet *sub judice*, though reported successfully by Beck<sup>20</sup> and recently demonstrated by Keyes, Jr.

Israel (*loc. cit.*) has stated that in the last 104 nephrectomies and nephrotomies performed since 1901 without the aid of methods of functional renal diagnosis he has had no deaths, and Rösing (*loc. cit.*) has reported 33½ per cent. of failures in cryoscopic findings controlled by operations. The reflex influence of a diseased kidney on its fellow may so influence its secretion as to make the freezing point ( $\Delta$ ) of urine lower, and the artifices resorted to in obtaining urine from the kidney also reflexly influence the flow of urine, causing a lowered freezing point. Barth,<sup>21</sup> therefore, correctly characterizes cryoscopy as of relative but not absolute value.

When, for reasons of renal insufficiency or other organic ailments, an operation seems contraindicated, we can hold out an amelioration of symptoms by observance of the hygienic and therapeutic measures practised in pulmonary tuberculosis, and, according to Madelung, Tuffier, Lancereaux, Koenig, Bangs, Ramsay, and Brown, cure is possible in very exceptional instances.

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## THE EFFECTS OF TRANSPOSITION OF THE DAILY ROUTINE ON THE RHYTHM OF TEMPERATURE VARIATION.

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ALTHOUGH it has been known for many years that the rhythm of the daily variations in body temperature is remarkably constant, no explanation advanced is accepted as adequate and entirely satisfactory. When the enormous number of thermometric observations continually made in medical practice is considered, it seems strange that more attention has not been paid to the physiological aspects of variations in temperature. The immediate effects of bodily exertion and muscular work have only lately been adequately appreciated; and with reference to the influence of many other factors like sleep, alimentation, etc., much confusion still exists. Certain features of the daily rhythm are generally recognized, such as the rise of temperature during the forenoon and afternoon, and the fall during the evening and early morning hours. A study of the literature<sup>1</sup> indicates considerable differences in the incidence of the maximum and minimum temperature, depending undoubtedly upon a variety of causes. Despite differences as regards dietetic habits, work, age, etc., the time of maximum temperature may be limited broadly between 4 and 8 P.M., and that of the minimum between 2 A.M. and 7 A.M., with an average range of variation of over 1° C. in rectal observations. While a hot or cold climate may determine minimal variations in the peripheral temperature of the body, the internal temperature, as measured in the rectum, appears to suffer only very slight modifications from such causes. The rise in temperature incidental to muscular exertion is transitory. The following quotations serve to indicate prevalent views regarding the diurnal rhythm. Dr. Pembrey writes: "As regards the causes of the daily variation in temperature, muscular activity and food appear to be the most important factors. In ordinary life man is most active and takes food during the day, and is least active during the night. . . . We may conclude that the daily variation in temperature is one of the features of a corresponding variation in the activity of the tissues of the body, as shown by the rate of the contraction of the heart, the frequency of respiration, the intake of oxygen, the output of carbon dioxide, the discharge of urea, and the capacity for muscular work."<sup>2</sup>

<sup>1</sup> An admirable review of the literature on this subject will be found in Pembrey's article in Schäfer's Text-book of Physiology, 1893, vol. i. p. 793, and in Richet's Dictionnaire de Physiologie article Chaleur, p. 91.

<sup>2</sup> Schäfer's Text-book of Physiology, 1893, vol. i. p. 801 *et seq.*

According to Prof. Richet, the daily variation of about  $1^{\circ}$  C. is "explicable en partie seulement par l'activité psychique et l'activité musculaire, et due surtout aux variations de tonicité du système nerveux régulateur de la chaleur." Jürgensen's observations on fasting subjects in which a more or less "normal" curve of temperature variations was maintained exclude the diet factor from a preponderating role. In estimating the relative importance of the bodily activities as distinguished from other environmental conditions, studies on the influence of the inversion of the daily routine have been made. The most recent are those of Benedict;<sup>1</sup> they claim special interest, because the observations were practically continuous over long periods of time. Such an arrangement was made possible by the use of a specially devised electric resistance thermometer reading to  $0.01^{\circ}$  C., which can be inserted 10 cm. to 15 cm. in the rectum and retained there without inconvenience during both waking and sleeping hours. Two subjects were carefully observed by Benedict: one a person usually working during the day, but made to work at night and sleep during the day for a series of consecutive days; the other, an individual long accustomed to night-work in the capacity of a night watchman. With reference to the first subject, Benedict concludes: "It is obvious that, at least with this subject, the influence of the inversion of the daily routine on the body temperature curve is noticeable only during the day, for while the evening fall, the early morning minimum, and the morning rise persist, the period of sleep during the day causes a marked fall of temperature, followed by a rise on awakening.

"The effect of the consecutive nights of night-work has not, therefore, succeeded in producing any marked disturbances of the curve between 6 P.M. and 8 A.M. By repeating the experiment and obtaining a curve after twelve consecutive nights of night-work, no greater tendency to influence the normal course of the curve, even after the somewhat longer period of work by night, is apparent.

"While the data of these two curves may warrant our regarding the temperature curve between 7 P.M. and 8 A.M. in a general way as fixed and independent of sleep or work (exempting severe muscular work), the curve during the remainder of the twenty-four hours—*i. e.*, 8 A.M. to 7 P.M.—undergoes marked alteration when sleep is taken in this period." Since this experiment indicated that the general form of the night curve is so firmly fixed as not to be materially altered, even after an inversion of the daily routine for ten or twelve days, the second experiment was conducted on a subject accustomed to a complete inversion of the daily routine for years. Prof. Benedict writes of this series of observations: "The remarkable course of these curves certainly cannot readily be explained as the result of influences ordinarily considered as affecting body

<sup>1</sup> Studies in Body Temperature, American Journal of Physiology, 1904, vol. xi. p. 145.

temperature. Obviously, we have here to do with some influences other than the ingestion of food, muscular activity, sleep, and body position. Of the main characteristics of the normal curve, the evening fall, the early morning minimum, and the morning rise are unmistakably found in both of these curves. The evening fall, though considerably diminished in amplitude, is sufficiently well marked to be easily recognized, and the early morning minimum and morning rise are likewise clearly seen. . . . It is thus seen that while years of night-work have not succeeded in eliminating the tendency to an evening fall, a minimum sometime during the night, and the morning rise, the whole course of the curve is markedly different from any with which we are familiar, and any study of the factors influencing the course of the curve must include a large number of experiments, in which the habits of life, times of eating, and muscular activity should all be as nearly alike as possible, in order to compare the results with the normal curves given by the several writers on body temperature."

From the preceding observations it has been assumed that the general form of the night curve remains practically intact, even when the daily routine is inverted, indicating a fixity of rhythm that is difficult to explain. As Benedict says: "Why the temperature of the human body reaches a minimum at 2 A.M. to 6 A.M., independent of whether the subject is sleeping soundly in the recumbent position or whether he is awake and sitting, or even standing and walking, is a problem that calls for extended research."

In view of the failure to note any marked inversion of the temperature curve by inverting the routine of life, it may be asked whether cosmic rather than bodily influences are the determining factors. Or, is the temperature rhythm a physiological function early established in the individual and largely independent of external impressions? Some light upon the question might be thrown by observing the changes of temperature rhythm which may attend the gain or loss of time incidental to a journey around the world. An opportunity to make a few notes on the subject was afforded the writer by a recent trip to the Philippine Islands. Manila time is approximately eleven hours earlier than that of New Haven. Accordingly, a journey from New Haven to Manila involves the shifting of the daily routine, so that day and night are practically reversed. What happens to the temperature curve?

The majority of the observations to be reported were made by the writer upon himself. Several persons in Manila (including one who made the same trip) permitted the collection of a few additional notes, which, however, I have not discussed in detail. Dr. Richard P. Strong, of the Insular Laboratory, has confirmed, in part, my own work by recording the temperatures of himself and of a second person and from observations on his patients. Major Bannister, in command of the First Reserve Hospital at Manila, has also fur-

nished me with some records obtained by a number of hospital-corps men on themselves.

All observations were made with the ordinary clinical one-minute thermometers. The limitations of the methods commonly employed are too well known to require discussion here. Rectal temperatures could be taken with convenience only in the writer's case. Temperature readings were made every two hours. Records made on the writer were kept for the whole day, as well as for both longer and shorter intervals; in the other experiments observations were continued for a part of the twenty-four hours only, but sufficient material can be obtained in this way to ascertain the characters of the curves. The readings by the hospital-corps men were, perhaps, not made with the care which is desirable in scientific work; however, trustworthy subjects were chosen and the records made on a large scale. *The precautions taken to make the results on the writer comparative* included usually the maintenance of the same bodily activity for an appropriate period before each temperature observation (except when sleeping). The thermometer was inserted 7 cm. to 8 cm. into the rectum for at least five minutes before each reading. Care was also taken to follow the same regular habits of life previously practised in New Haven.

## TRANSPOSITION EXPERIMENTS ON R. B. G.

*Itinerary of the Trip.* The start from New Haven was made on June 24th and the arrival at Manila occurred August 1st; the time required for the trip over was, therefore, thirty-seven days. The return from Manila began September 15th; Nagasaki to the north was left a week later, and the journey ended at New Haven on November 1st, forty-eight days after sailing from the Philippines. Short stops of a day or two at Chicago, San Francisco, Honolulu, and Guam delayed somewhat the trip westward; and a few days at Nagasaki, San Francisco, St. Louis, and Chicago also prolonged the time of travel for the return to New Haven.

*Control experiments* for a period of two days, June 21st, 7 A.M., to June 23d, 7 A.M., were made just before leaving New Haven. The resulting curves (Chart I.) are practically normal in character.

### CHART I.



The broken line in this and the following charts is the record of the control, New Haven observations; the other, the Manila observations of August 5th, 6th and 7th.

There is a tendency for the temperature to be somewhat high in the morning, but this is not an unusual observation. The maximum at 5 o'clock in the afternoon, the evening fall, the early morning

minimum (1 A.M. to 3 A.M.) and subsequent rise, and the range of variation are typical. The summary of the observations follows:

	Maximum.	Minimum.	Temp. range.	Mean.
June 21-22 (24 hours)	37.9°+ (5 P.M.)	36.8° (1 and 3 A.M.)	1.1°	37.4°
June 22-23 (24 hours)	37.8 — (11 A.M.) 37.7 — (5 P.M.)	36.7 (1 A.M.)	1.1 —	37.3

*Observations at Manila* were made in three periods, with intervals of about three weeks:

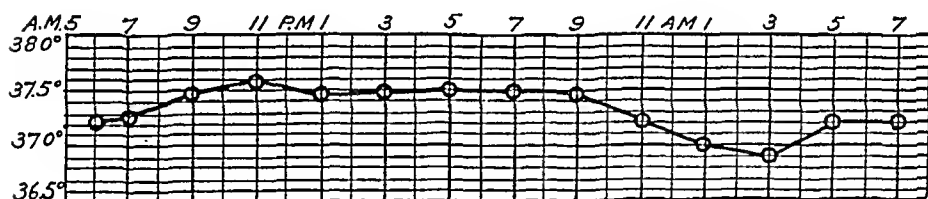
1. The first series (Temperature Chart I.) was begun four days after landing. The observations for this period afford a typical "normal" curve. The maximum is somewhat earlier in the afternoon than in the New Haven controls. The temperature range is little over half that in New Haven. There is a slight morning fall:

	Maximum.	Minimum.	Range.	Mean.
August 5-6 (5 A.M.-7 A.M. 26 hours)	37.6°—(3 and 5 P.M.)	37.0° (1 and 3 A.M.)	0.6°	37.3°
August 6 (7 A.M.-9 P.M.)	37.7— (5 P.M.)	.....	.....	.....
August 7 (5 A.M.-9 P.M.)	37.7— (3 P.M.)	.....	.....	.....

2. These results (Chart II.) for August 22d and 23d are of the same character as the preceding series:

	Maximum.	Minimum.	Range.	Mean.
August 21 (9 A.M.-5 P.M.)	37.7° (3 P.M.)	.....	.....	.....
Aug. 22-23 (6 A.M.-7 A.M. 25 hours)	37.6 (11 A.M.) 37.5 (5 and 7 P.M.)	36.9° (3 A.M.)	0.6°	37.3°

CHART II.

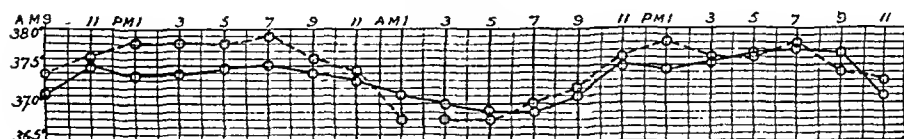


Observations at Manila, August 22d and 23d.

3. The third set of observations (Chart III.) for September 9th and 10th show no noteworthy differences from the two series previously recorded:

	Maximum.	Minimum.	Range.	Mean.
Sept. 9-10 (7 A.M.-7 A.M. 24 hours)	37.5° (9 A.M. and 5 P.M.)	36.9° (3 and 5 P.M.)	0.6°	37.3°—
Sept. 10 (7 A.M.-9 P.M.)	37.7° (5 P.M.)	.....	.....	.....

CHART III.



Manila, September 9th and 10th.

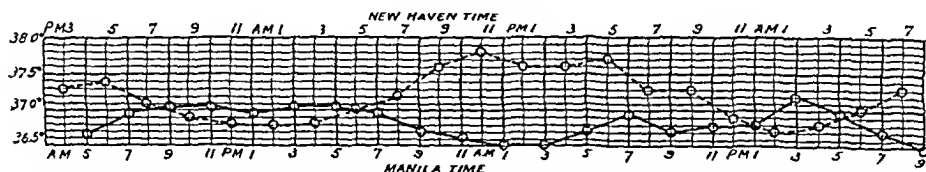
<sup>1</sup> This high figure is associated possibly with some slight bodily exertion prior to recording the temperature.]

It is seen from the charts of the observations given above that the general form of the Manila curve corresponds in outline closely to the course of a typical temperature record. The morning rise, the late afternoon maximum, the characteristic evening fall, and the early morning minimum—all these important variations are found to occur much as usual. Even before the writer was accustomed to retire (shortly after 11 P.M.), the evening drop was well down toward the minimal figure for the twenty-four hours. A comparison of the Manila and the New Haven control curves brings out in a very forcible manner the analogy of the one set with the other. Some features of the above observations deserve, however, to be examined more fully in detail.

A slight, though noticeable, lowering of the temperature in the morning is a somewhat persistent character throughout the three series. However, variations of the same nature are not uncommonly met with in normal observations (see, for example, the controls and the later New Haven records). In fact, a rapid morning rise succeeded by a slight fall is so prominent a feature in the results of former temperature investigations that it has led in the past to some uncertainty regarding the actual time of the daily maximum.<sup>1</sup> It is improbable, therefore, that the slight fall is produced by the continued existence of the coincident evening temperature depression found in the earlier New Haven curve. In the inversion experiments of both U. Mosso<sup>2</sup> and Benedict, the evening fall persists to a very much more striking degree, and follows fairly closely the line of the normal control curve.

The daily temperature range ( $0.6^{\circ}+$ ) is unusually limited; it is somewhat over half that observed in New Haven. The difference between the New Haven and the Manila maxima (about  $0.2^{\circ}$ ) is practically the same as that of the respective minima, so that a medial abscissa to a set of the Philippine extremes occupies the same relative position to the limits of the New Haven variations. If the Manila curves and the controls are plotted together (Chart IV.), so

CHART IV.



New Haven controls and Manila records of August 5th and 6th; plotted eleven hours apart.

that the succession of simultaneous events in the two places is comparable, it will be seen that the two sets of observations are practically exactly reversed. It might be argued, accordingly, that the

<sup>1</sup> Pembrey. . Schäfer's Text-book, vol. i. p. 793.

<sup>2</sup> Arch. ital. d. biologie, 1887, vol. viii. p. 177.

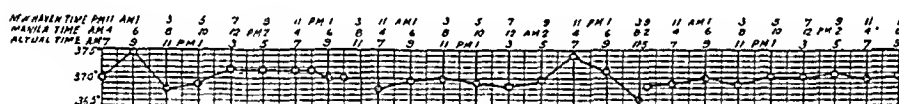
small range may be due to an antagonistic influence exerted by the persistence, to some degree, of the original New Haven characters. Later observations during the return trip (*vide infra*) indicate, however, that this cannot be the case. The explanation of the limited variation must be sought probably in the changed environment; it is to be found presumably in the new climatic conditions and the quieter life of the tropics.

In the five and a half weeks from the first to the third series of observations, the character of the curves underwent no noteworthy alterations. The mean temperature for the day remained practically uninfluenced by the transposition.

Observations during the return journey were made to ascertain if the daily change of twenty minutes or so in time had any immediate effect on the typical rhythmic variations. The return curves were found to be apparently independent of the possible persistence either of the Manila or the New Haven characters. The temperature variations seem to be adjusted to the gradual transposition of routine forced upon the body by the nature of the trip:

1. The first of the two series was made on October 1st, 2d, and 3d, between longitude 165° east and 180°; the actual time was, therefore, eight and one-third to seven and two-thirds hours earlier than that of New Haven, and three to three and two-thirds hours later than at Manila. The curves are given in Chart V.

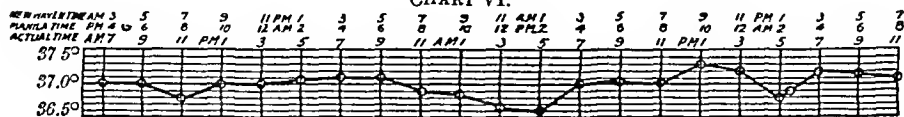
CHART V.



Return journey, October 1st, 2d, and 3d.

2. Observations were made October 14th and 15th between longitude 134° west to 129° west (Chart VI.); the time was four and

CHART VI.



Return journey, October 14th and 15th.

one-third to four hours earlier than at New Haven. A summary of the twenty-four hours, beginning October 14th, at 7 A.M., follows:

Maximum.	Minimum.	Range.	Mean.
37.1° (7 and 9 P.M.)	36.3° (5 A.M.)	0.5°	36.9°

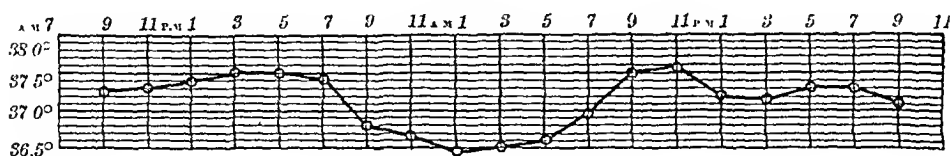
The temperature variations in both series show a tendency to be unusually limited—a condition of affairs probably associated with the sedentary character of the life as a passenger on a transpacific

steamer for some length of time. Some abrupt and apparently unexpected variations are found in the first set, but these are capable of explanation. Thus, the sudden elevation on the morning of October 1st (Chart V.) is possibly associated with a rather vigorous walk on deck, followed by an unusually hearty breakfast, though the writer had been quiet for at least an hour before the observation at 9 A.M. The high figure at 7 P.M. on October 2d may also have been influenced by activity some little time previous to taking the temperature; the functional processes were probably aroused through unusual exertion from a lethargy induced by the character of the life aboard ship. To prevent possible variations of this sort was one object of the experiment on October 3d, in which a uniform (and quiet) state of bodily activity was maintained so far as practical during the day. The record shows an unusually small temperature change, though otherwise the curve presents the "normal" characters.

If the above explanation of these variations can be accepted, the records of October 1st and 2d are fairly regular. At least they fail to show any persistency either of the Manila or the original New Haven influences.

The later observations on the 14th have the time of the maximum and minimum points occurring about two hours later than might be expected from a consideration of the character of the previous observations. In fact, the first half of the curves of this series follows closely the actual time relations of the New Haven controls. The small temperature range ( $0.5^{\circ}$ ) for the first twenty-four hours cannot here be due to any antagonistic influences of the original rhythm. The rest of the record on October 15th would probably have been of the ordinary type throughout if the writer had not inadvertently fallen asleep between 3 and 5 o'clock in the afternoon. The fall in the curve for this period is coincident with the condition of physical and mental depression.

CHART VII.



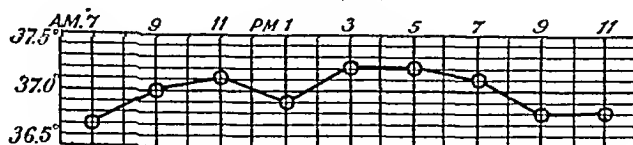
November 3d and 4th at New Haven.

Observations on arrival at New Haven were recorded on November 3d, 4th, and 6th. The curves (except November 4th) are normal in character and resemble the earlier New Haven observations closely. The thermo-regulatory mechanism has been readjusted to the former conditions. The mean temperature, however, is low. The curves are plotted in Charts VII. and VIII.



	Maximum.	Minimum.	Range.	Mean.
Nov. 3-4 (7 A.M.-7 A.M.)	37.5° (3 and 5 P.M.)	36.4+° (1 A.M.)	1.1°—	37.0°
Nov. 4 (7 A.M.-9 P.M.)	37.5 + (11 A.M.)	.....	....	.....
	37.3 (5 and 7 P.M.)			
Nov. 6 (7 A.M.-11 P.M.)	37.2 (3 and 5 P.M.)	.....	.....	.....

CHART VIII.



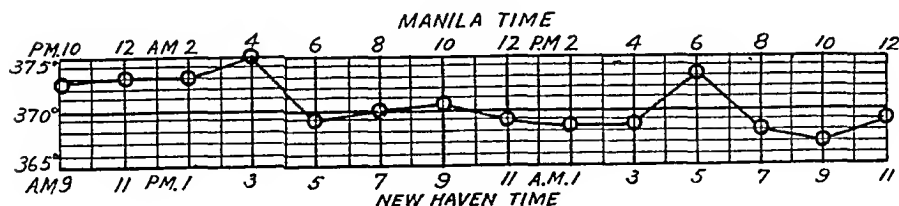
November 6th at New Haven.

*Inversion of the Manila routine* should give a result practically of the same character as the New Haven observations if the original rhythm can still persist uninfluenced by the transposition. Difficulties made such an experiment unpractical in Manila, but the attempt was made on shipboard between that city and Nagasaki, which lies almost to the north of the islands.

The experiment was so arranged that the routine should correspond almost exactly with the New Haven program. Only a few hours' sleep were taken on the night of September 17th and 18th, and the latter part of the morning and the afternoon were spent in slumber. Temperature observations were begun at 10 P.M. on this day. Sleep on the 19th was fairly good, but the writer became very tired at night, notwithstanding the six or seven hours' rest. As comparable bodily conditions were not being maintained, the experiment was interrupted, and, unfortunately, could not be repeated. The curve is plotted in Chart IX., and the summary for the day follows:

Maximum.	Minimum.	Range.	Mean.
37.5° (4 A.M.)	36.7° (10 P.M.)	0.8°	37.0°
(N. H. time = 3 P.M.)	(N. H. time = 9 A.M.)		

CHART IX.



Inversion experiment.

The curve resulting from the inversion is somewhat difficult of interpretation. The characteristic night depression apparently had not occurred to any extent when temperature observations were begun. The maximum figure coincides fairly well with the time for the occurrence of the corresponding New Haven variation. Though not quite typical, the rapid depression in the morning (3 P.M. to

5 P.M., New Haven time) is somewhat suggestive of the early evening fall in the original curve; certainly, it is not characteristic of the Philippine records. The later observations seem to be referable rather to a readjustment of the Manila conditions, modified somewhat by the unusual state of the bodily activities during the late morning and afternoon. After a refreshing sleep, the temperature rises suddenly to a figure which corresponds with the ordinary Manila reading at this hour, but which is also coincident with the New Haven morning elevation. The usual evening fall then manifests itself. The subsequent slight rise at midnight is the result probably of an attempt to throw off the physical and mental depression occurring notwithstanding the sleep obtained during the day. On the whole, the experiment does not exclude but rather suggests the possibility of a return of the temperature rhythm in part to the New Haven character if comparable conditions of inversion are maintained.

#### OBSERVATIONS ON OTHER SUBJECTS.

In a series of observations on other individuals all the precautions desirable to avoid the occurrence of preventable error could not be taken. Comparable conditions of the body as to sleep, time of eating, exercise, etc., were frequently not obtainable. The readings were occasionally made at irregular intervals, and are over shorter periods than the writer employed in his own case.

The temperature record of the other subject who made the trip from New Haven to Manila comprises controls for a period of two days and two sets of observations in the Philippines. The New Haven variations (axillary temperatures) were perfectly normal in character. The Manila experiments (both axillary and sublingual readings), like the results on the writer, show an apparent adjustment of the temperature variation to the new conditions. Though a month apart in point of time, no essential differences were noted between the series made shortly after landing and the later set of observations.

Additional collected data corroborate the facts already presented. Thus, curves were obtained of the daily temperature variations in two individuals who have resided in the islands for two and a half years and who originally went over from this country. The results here indicate a permanent adjustment to correspond with the transposition of routine.

Temperature observations were also made by Dr. Strong, of the Insular Biological Laboratories, on himself and others who had resided for various lengths of time in Manila. The rise during the morning and early afternoon was found to occur as usual and was normal in character. No trace of the persistence at Manila of the original evening fall was apparent in Dr. Strong's experiments. Finally, the temperature records of eight hospital-corps men (on both

day and night details) give no evidence that transposition of routine affects the daily rhythmic variations in a manner other than has been already described.

The daily rhythmic temperature variation has been shown to be shifted in point of time. It is, therefore, capable of being shifted at least gradually. Why, then, does not inversion of the routine produce a corresponding alteration in the temperature curves obtained under these conditions? In the course of the present investigation the existence of some relationship between the functional "tone" of the body and the variations in the temperature record has repeatedly been impressed upon the writer. For instance, whether beginning at 7 P.M. or at 11 P.M., the first portion of the evening temperature fall seems to be coincident with the onset of a state of physical and mental depression. It is possible that the explanation of Benedict's results is to be found in the depressing effects of environmental conditions, such as darkness, artificial illumination, the unusual absence of noise and external activity, and in the habitual and regular reactions of the body to these influences.

SUMMARY. The transposition of the daily routine through a period of practically half a day, experienced as the result of the time changes during the trip from New Haven to Manila, was accompanied by an immediate adjustment of the rhythmic temperature variation to the new régime in the case of the writer and of a second subject, so that on arrival in the islands the curves obtained were still "normal" in character.<sup>1</sup> Subsequent residence in the Philippines for a period of about six weeks induced no alterations of any significance. Observations (on the writer alone) made during the return trip showed an apparent adjustment of the temperature rhythm day by day coincident with the shifting of the routine. After returning to New Haven the record continued to be normal and resembled closely the earlier controls. Inversion of the Manila program seems to prevent the usual evening fall and early morning minimum, if comparable bodily conditions are maintained; the single experiment on the writer, however, is an inadequate basis for a positive statement. Additional observations on individuals who came originally from the United States, and who have resided in Manila for varying periods of time, corroborate in part the results on the writer, in so far as the temperature rhythm was found to be of the ordinary type. No evidence has been obtained that any of the Manila temperature variations are associated with the persistence of the original normal features, a result contrary to the facts brought out by Benedict's experiments on routine inversion. Transposition of the daily routine, therefore, appears to produce a corresponding and coincident shifting of the rhythmic temperature changes, so that the normal character of the variations is always preserved.

<sup>1</sup> Except for a somewhat limited daily range of variation.

It is to be hoped that one result of the publication of the present paper will be to draw attention to a subject of considerable physiological interest and importance. The observations need to be corroborated and extended. Additional data should be furnished concerning the effects of transposition and inversion of the daily routine, not only on temperature, but on other rhythmic functional variations as well.

I desire to express my indebtedness to Prof. Mendel, of this laboratory, for suggestions offered, and to Dr. Strong, of the Insular Biological Laboratories, and Major Bannister, of the United States Army, for their interest and helpful co-operation.

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## A STUDY OF THE METABOLISM OF A VEGETARIAN.

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(From the Laboratory of Physiological Chemistry, University of Pennsylvania.)

THE patient, a student in one of the departments of the University of Pennsylvania, on whom the observations here reported were made, consulted me on March 10, 1903, complaining of a mild infection of the respiratory tract. He was then twenty years old, tall, anæmic-looking, and not at all robust in make-up. During the course of my examination I determined that the infection was not of a tuberculous nature, and learned that the patient was the son of vegetarian father and mother, and that his grandparents had also been vegetarians, as he was himself. I induced him to weigh and record the articles of his diet, to furnish me with his entire twenty-four hours' urine, and to keep a record of his body weight daily for a week. He also submitted samples of the milk that he drank, so that I might determine the amount of nitrogen that he was ingesting with this article of diet, the only animal food that he took.

From the submitted twenty-four hours' urine I determined (1) the total volume passed, (2) the amount of nitrogen excreted, with its equivalent in urea, using the Kjeldahl method, and (3) the phosphorus excretion expressed as  $P_2O_5$ , using the uranium acetate method.

From the diet lists submitted I calculated the amount of nitrogen ingested with the food as follows: The Kjeldahl method was used on five specimens of milk, thus giving an accurate estimate of the amount of nitrogen ingested with that food. From these five determinations an average was taken, and the nitrogen in the remainder of the milk used, samples of which, for one reason or another, could not be obtained, was estimated, using that average as a basis. The

nitrogen-content of the other articles of diet was calculated from Atwater's tables.<sup>1</sup>

There are certain unavoidable inaccuracies in this study, on account of the fact that the subject was human and could not be absolutely controlled. These inaccuracies are: 1. That already referred to concerning the nitrogen-content of certain of the specimens of milk. 2. The absence of analyses of certain substances used by this individual in his diet; for instance, ginger wafers, cookies, and other cakes, of which the subject partook freely, are all grouped in the diet lists as cake. The nitrogen factor used was that of the average of all the cake examined as given in the above-mentioned tables. Again, no analysis of peanut-butter was accessible, and the factor selected for the nitrogen in that article was that given in Atwater's tables for peanuts. Bread, toast, and rolls are all tabulated as bread, and the nitrogen factor adopted was that obtained by averaging the protein percentage in the tables for white bread and white wheat rolls. On one occasion the subject ate five cents' worth of ice-cream; this does not appear in the determinations, nor is any account taken of the nitrogen of cream chocolate, which he ate freely. 3. A third source of inaccuracy lies in the fact that the amount of nitrogen eliminated in the feces was not determined.

1. **THE DIET.** The diet of the individual under consideration consisted in the main of white wheat bread, of rolls made of white wheat flour, with butter, potato, milk, and some form of cake. These articles he ate daily. He varied his diet by adding to it on different days celery, corn, crackers, peanut-butter, cream chocolate, apple, orange, and Graham wafers. The daily amount of nitrogen ingested with these articles determined by the methods stated above varied between 11.33 grams and 7.534 grams, corresponding to a protein ingestion of between 70.812 grams and 47.087 grams. During the week he ingested 65.396 grams, corresponding to 408.725 grams of protein, or an average of 9.342 grams daily, corresponding to 58.387 grams of protein.

The amount of protein food necessary for the proper nutritive equilibrium of man has been variously estimated by different observers. Voit, whose results have been most extensively quoted, believes that the daily diet should contain 118 grams of protein food, which is equivalent to 18.88 grams of nitrogen. Atwater,<sup>2</sup> whose studies have been made principally on Americans, believes 125 grams of protein food are necessary for a man doing moderate muscular work, an equivalent of 20 grams of nitrogen daily.

2. **THE NITROGEN OUTPUT.** The nitrogen excreted in the urine varied from day to day; on some days it was greater than the amount ingested, and on other days it was less than the amount ingested. The highest excretion was 12.0204 grams; the lowest 7.476 grams; an average of 9.8192 grams per day. The total nitrogen excretion for the week was 68.735 grams, or 3.339 grams more than was

ingested. If we accept 30 grams of urea as the normal output of an adult man, the equivalent in nitrogen would be 13.9 grams; if now we add something to this to allow for nitrogenous bodies other than urea, 15 grams would probably represent the normal nitrogen excretion daily; a figure considerably in excess of the amount of nitrogen excreted by the subject.

More important than this, however, is the fact that in the urine alone the subject was excreting more nitrogen than he was ingesting. Suppose we add 0.5 gram as the nitrogen daily excreted by the feces and the sweat; then in one week the subject excreted 7.8 grams more nitrogen than he ingested—a condition of affairs not calculated to produce a robust and mentally and bodily active individual.

3. THE PHOSPHORUS OUTPUT. The phosphorus excretion (calculated as  $P_2O_5$ ) varied between a maximum of 1.7303 and a minimum of 1.158; it averaged 1.5653 for the week, a quantity smaller than that which is said to be present in the normal urine. The relation of the phosphorus excretion to the nitrogen excretion was as 1 to 5.9, 1 to 7.1, 1 to 5.5, 1 to 7.7, 1 to 6.1, 1 to 6.4, and 1 to 6.1.

4. THE WATER INGESTED AND THE URINE EXCRETED. During the week that he was under observation the subject drank 7915 c.c. water, an average of 1130.7 c.c. daily. To this must be added the water taken with the food. For example, there is about 87 per cent. water in milk, of which the subject drank 4694 c.c. during the week, in which there would be 4083.78 c.c. water. The subject, therefore, ingested more than 11,998.78 c.c. water during the week, or more than 1714.11 c.c. daily. During this period he passed 7560 c.c. urine, an average of 1080 c.c. daily. According to this calculation, 634 c.c. water must have been eliminated daily by the feces, sweat, and as vapor of water from the lungs, or some of it must have been retained in the body.

The influence of water on the metabolic processes is said by some observers to stimulate metabolic activity and to assist in washing out the products of metabolism from the tissues. (Halliburton.<sup>3</sup>) Others state that water increases the waste nitrogenous products (Gruber<sup>5</sup>), while Straub<sup>6</sup> found that removal of water from the food increases protein katabolism, as shown by an increase of the excretion of both nitrogen and phosphorus. Neumann, on the other hand, says that large quantities of water have no influence on metabolism other than to flush out the products of katabolism.

5. THE WEIGHT. By a reference to the table it will be seen that the weight of the individual who was the subject of this study varied between a maximum of 65.3 kilograms (144 pounds) and a minimum of 64.5 kilograms (142½ pounds).

It is admitted by everyone that nitrogen is essential for the maintenance of human life and metabolic activity. The questions in dispute are: 1. Whether the nitrogen contained in vegetable food is as valuable as an element of nutrition as that contained in animal

food, particularly in meat. 2. Whether the bodily functions of an individual using vegetable nitrogen exclusively are conducted in a normal manner. 3. The amount of nitrogen required daily by a human subject for the best results of growth and of bodily and mental function. It has been claimed by some (Davis<sup>7</sup>) that the protein contained in vegetable food is less easily digested than that of meat; this has been denied by others. The probability is that the protein itself is just as easily digested if it come from one source as from the other; but that the proportion of protein, bulk for bulk, renders that contained in animal food more readily available.

In this connection, some experiments made by Rockwood<sup>9</sup> are of interest. He found that vegetable proteins are not utilizable to the same extent as those of animal origin, unless they are removed from the materials associated with them. The degree of utilization, however, is found to be slightly increased by long cooking. In one experiment extracted vegetable protein showed itself capable of as great utilization as that of animal protein; in another experiment less so.

The strict vegetarian must take a large bulk of vegetable food in order to obtain the quantity of protein required for the needs of his tissues. The large quantity of carbohydrate ingested in order to procure the necessary protein must be a hindrance to normal body chemistry, on account of the fermentations that are likely to take place in the intestinal tract. Writers seem to be agreed that the use of a strictly vegetable diet; while it may permit of a normal amount of work at times, will not permit of sustained effort, nor will it allow users to meet sudden calls for increased exertion. Furthermore, it has been shown that strict vegetarians lose vigor, become languid, and are not inclined to do severe mental and physical work (Davis,<sup>7</sup> Parkes,<sup>4</sup> Halliburton<sup>3</sup>).

In the case under review the anæmic and delicate appearance of the subject, together with the fact that his college work was below the average of efficiency, would point to a deficient diet, although the influence of other possible causes have not been overlooked.

The amount of nitrogen required by the human subject in twenty-four hours for the best performance of body function is variously estimated: According to Moleschott, 130 grams of protein, equivalent to 20.8 grams of nitrogen; according to Ranke, 100 grams of protein, equivalent to 16 grams of nitrogen; according to Voit, 118 grams of protein, equivalent to 18.88 grams of nitrogen; according to Forster, 131 grams of protein, equivalent to 20.96 grams of nitrogen; according to Atwater,<sup>1</sup> 125 grams of protein, equivalent to 20 grams of nitrogen, are required daily. Halliburton<sup>3</sup> places the necessary daily nitrogen at 15 grams. Sivé<sup>n</sup><sup>8</sup> found, however, that for a short time an adult, without increasing the total heat value of the food beyond the normal, can remain in nitrogen equilibrium and

good working condition with an income of nitrogen of only 4.52 grams, or 28.25 grams of protein. We may assume, in spite of this abnormally low figure, that between 15 and 20 grams of nitrogen, corresponding to 93.75 to 125 grams of protein, are required daily by a man doing ordinary work. The subject of this study was taking much less than the minimum requirement.

CONCLUSIONS. 1. A male, aged twenty years, took habitually a diet composed of white wheat bread or rolls made of white wheat flour, with butter, potato, some form of cake, celery, corn, crackers, peanut-butter, cream chocolate, apple, orange, Graham wafers, and milk, the last being his only article of food of animal origin. By the use of this diet he ingested an average of 9.342 grams of nitrogen daily, corresponding to 58.387 grams of protein. During the period of observation he excreted in his urine an average of 9.8192 grams of nitrogen daily, equivalent to 21.032 grams of urea daily. During the entire period he excreted 3.339 grams more nitrogen in his urine than he ingested with his food. He excreted an average of 1.5653 grams of  $P_2O_5$  daily. He ingested an average of 1130.7 c.c. of water daily, to which the addition of the water in the milk drunk would bring the daily average of water taken to 1714.11 c.c. He passed an average of 1080 c.c. of urine daily. His weight was maintained between 64.5 kilograms (142½ pounds) and 65.3 kilograms (144 pounds).

2. The study of the patient seems to show that, for this individual at least, the diet was not calculated to produce a properly nourished and mentally and bodily active individual. There are undoubtedly strong and robust individuals who live on a very simple diet; but I believe that such are the exception rather than the rule. The average book, pamphlet, or magazine article advocating vegetarianism, so far as I have been able to examine such, contains no accurate scientific analysis of the requirements of the human organism, and the arguments advanced for the adoption of such a regimen are pseudo-scientific or sentimental.

March 15, 1903.

Diet.	Weight in grams.		Nitrogen in diet.
Bread . . . . .	119	Bread . . . . .	3.121
Potato . . . . .	127	Potato . . . . .	0.548
Cake . . . . .	127	Cake . . . . .	1.422
Celery . . . . .	14	Celery . . . . .	0.031
Corn . . . . .	92	Corn . . . . .	0.413
Gingerbread . . . . .	10	Gingerbread . . . . .	0.086
Crackers . . . . .	49	Crackers . . . . .	0.765
Peanut-butter . . . . .	35	Peanut-butter . . . . .	1.448
Milk* . . . . .	701	Milk* . . . . .	3.495
Butter . . . . .	31		
		Total . . . . .	11.330

\* Nitrogen in milk determined from averages of actual analyses.



## March 16, 1903.

Diet.	Weight in grams.		Nitrogen. in diet.
Bread . . . . .	205	Bread . . . . .	1.442
Potato . . . . .	297	Potato . . . . .	1.283
Crackers . . . . .	35	Crackers . . . . .	0.548
Peanut-butter . . . . .	21	Peanut-butter . . . . .	0.866
Cake . . . . .	56	Cake . . . . .	0.627
Butter . . . . .	42	Milk* . . . . .	3.989
Milk* . . . . .	785		
		Total . . . . .	8.755

## March 17, 1903.

Bread . . . . .	235	Bread . . . . .	3.684
Potato . . . . .	241	Potato . . . . .	1.041
Crackers . . . . .	35	Crackers . . . . .	0.548
Peanut-butter . . . . .	21	Peanut-butter . . . . .	0.866
Cake . . . . .	49	Cake . . . . .	0.548
Cream chocolate . . . . .	28	Milk† . . . . .	3.882
Butter . . . . .	63		
Milk† . . . . .	779	Total . . . . .	10.569

## March 18, 1903.

Bread . . . . .	205	Bread . . . . .	3.214
Potato . . . . .	191	Potato . . . . .	0.825
Crackers . . . . .	50	Crackers . . . . .	0.784
Peanut-butter . . . . .	28	Peanut-butter . . . . .	1.154
Cake . . . . .	49	Cake . . . . .	0.548
Cream chocolate . . . . .	49	Milk† . . . . .	3.075
Butter . . . . .	56	Milk* . . . . .	1.366
Milk† . . . . .	617		
Milk* . . . . .	283	Total . . . . .	10.966

## March 19, 1903.

Bread . . . . .	262	Bread . . . . .	4.111
Potato . . . . .	142	Potato . . . . .	0.613
Cake . . . . .	70	Cake . . . . .	0.784
Orange . . . . .	36	Orange . . . . .	0.046
Cream chocolate . . . . .	71	Milk* . . . . .	1.190
Butter . . . . .	70	Milk† . . . . .	1.520
Milk* . . . . .	233		
Milk† . . . . .	305	Total . . . . .	8.264

## March 20, 1903.

Bread . . . . .	226	Bread . . . . .	3.543
Potato . . . . .	312	Potato . . . . .	1.347
Graham wafers . . . . .	21	Graham wafers . . . . .	0.329
Cake . . . . .	42	Cake . . . . .	0.470
Apple . . . . .	135	Apple . . . . .	0.108
Butter . . . . .	49	Milk* . . . . .	2.181
Milk* . . . . .	432		
		Total . . . . .	7.978

## March 21, 1903.

Bread . . . . .	213	Bread . . . . .	3.339
Potato . . . . .	163	Potato . . . . .	0.704
Cake . . . . .	63	Cake . . . . .	0.705
Cream chocolate . . . . .	149	Milk† . . . . .	2.786
Butter . . . . .	42		
Milk† . . . . .	559	Total . . . . .	7.534

\* Nitrogen in milk determined by Kjeldahl's method.

† Nitrogen in milk determined from averages of actual analyses.

Date.	Nitrogen in diet.	Protein in diet.	Nitrogen in urine.	Equivalent in urea.	Water ingested.	Water ingested as milk.	Urine passed.	P <sub>2</sub> O <sub>5</sub> excreted.	Weight.
March 15	11.330	70.812	10.395	22.275	1500 c.c.	609.87 c.c.	1650 c.c.	1.749	64.8 k. (142 $\frac{3}{4}$ lbs)
" 16	8.755	54.718	9.2046	19.7242	907 "	682.95 "	1105 "	1.2818	64.8 k. (142 $\frac{3}{4}$ lbs)
" 17	10.569	66.056	9.5711	20.5095	985 "	677.73 "	1210 "	1.7303	64.8 k. (142 $\frac{3}{4}$ lbs)
" 18	10.966	68.537	12.0204	25.7580	1155 "	783.00 "	1080 "	1.674	64.5 k. (142 $\frac{1}{4}$ lbs)
" 19	8.264	50.650	10.6543	22.8307	998 "	468.06 "	1095 "	1.7191	65.3 k. (144 lbs)
" 20	7.978	49.862	7.476	16.02	1071 "	375.84 "	600 "	1.158	64.8 k. (142 $\frac{3}{4}$ lbs)
" 21	7.534	47.087	9.4136	20.172	1299 "	486.33 "	820 "	1.5252	64.9 k. (143 lbs)
Total	65.396	407.722	68.735	147.2694	7915 "	4083.78 "	7560 "		

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## ON THE DETECTION OF MINUTE TRACES OF SUGAR IN THE URINE.

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PRACTICALLY all authorities admit that traces of sugar may occur in the urine of perfectly normal individuals, especially if the ingestion of carbohydrates has been excessive. Although such traces do not concern the average practitioner, since the condition giving rise to their presence is scarcely pathological, it is of interest scientifically to consider how these minute quantities of sugar may be detected, and notably so since methods of such detection are not discussed by the various authorities on urinalysis. In fact, that the test hereinafter considered actually demonstrates the presence of minute quantities of sugar in urine is not generally accepted, and it is the purpose of this paper to show why such delicacy may properly be attributed to it.

In 1884 Emil Fischer<sup>1</sup> first called attention to the fact that phenylhydrazin, in combination with certain carbohydrates, formed definite and characteristic crystalline compounds. His work upon the subject was scientific and quite exhaustive, though he barely more than suggested a practical application. A few years later von Jaksch and Grocco gave the test its introduction as a clinical procedure, and to the former is due largely the high esteem in which it has been held as a means of detecting sugar in glycosuria. It has since been studied by a number of investigators, notably among the Germans, but conclusions thus far have not been entirely uniform.

Briefly speaking the test consists in treating a portion of suspected urine in a test-tube with phenylhydrazin hydrochlorate and sodium acetate, heating, cooling, and allowing the tube to stand for some time, then examining the resulting sediment microscopically. As to the proportion of ingredients used nearly all authorities are agreed, recommending that 10 c.c. of urine be mixed with 1 gm. of phenylhydrazin and 2 gms. of sodium acetate. Regarding the manner and duration of boiling, opinions differ. Fischer used a water bath, boiling the tube ten to fifteen minutes; von Jaksch proceeded similarly, but boiled the tube longer. Hirschl<sup>2</sup> claimed that by boiling in a water bath one hour an absolute differentiation between glucose and glycuronic acid could be made; while Williamson<sup>3</sup> considered that prolonged heating introduced certain fallacies and advised that the test-tube be boiled for two minutes only, directly over the lamp. All are quite agreed that prolonged standing serves to bring out the crystals more perfectly. Disregarding these differences of opinion as to details, we may say that the accepted method of applying the test to-day is as follows: To 10 c.c. of urine in a test-tube 1 gm. of phenylhydrazin hydrochlorate and 2 gms. of sodium acetate are added; the tube is heated in a boiling water bath for one hour; it is then allowed to stand twenty-four hours, when a microscopic examination of the sediment at the bottom of the tube is made; if sugar has been present in the urine, certain yellow crystalline forms are to be seen.

It is at this point that confusion and doubt have arisen, for the crystals produced are not of one uniform type. A survey of the literature discloses that the crystals constantly mentioned as present are divisible into two general types. One of these is universally acknowledged to be the genuine phenylglucosazone crystal, and is described as being composed of delicate, sulphur-yellow needles, beautifully arranged in sheaves, half-sheaves, rosettes, and sprays. Its appearance is proof positive of the presence of sugar. The other type is that of a much smaller crystal of the same color, a conception of its form and appearance being quite accurately conveyed by the word "thornapple," meaning thereby the seed-

pod of *Datura stramonium*. It is seen in short, boat-shaped staves with few or many centrally disposed radiating spiculæ, and has been likened, save for its color, to the crystal of ammonium urate, neutral calcium phosphate, and hippuric acid. It has been observed repeatedly by different investigators in diabetic urine, in artificially saccharine urine, and in normal urine, after the application of the phenylhydrazin test. Approximately three views are held as to the significance of this crystal: first, that it is to be disregarded totally as having no import;<sup>5</sup> second, that it indicates the presence of glycuronic acid or some unknown constituent of urine;<sup>9</sup> third, that it signifies the certain presence of sugar.

Considering these views seriatim it may be said, with respect to the first, that the crystal has some import, since in many specimens examined it is not found. Its presence or absence therefore indicates the presence or absence of some urinary constituent.

The second view is more vital. Glycuronic acid forms with phenylhydrazin yellow crystals which are scarcely to be distinguished microscopically from those of glucosazone. Thierfelder<sup>9</sup> investigated this combination extensively. Later Hirschl<sup>2</sup> described the glycuronic acid phenylhydrazin crystals as follows: "Out of a central mass many needle-like spiculæ project, to become merged immediately into other and similar masses; the centre of the radially arranged needles appears as an irregular mass out of which the needles seem to be growing." Jolles<sup>8</sup> accepts this description, but adds that the glycuronic acid crystals are shorter and thicker than the sugar crystals, and are never so regularly arranged; their disposition is generally in rosettes, approaching in appearance the thornapple type; he emphasizes the statement that the glucosazone crystals are long and slender as compared with the acid crystals.

The experiments which the writer has made confirm in the main the accuracy of Hirschl's description of the glycuronic acid crystals. In the majority of tests made aqueous solutions of glycuronic acid treated with phenylhydrazin (in the same manner as urine) gave a greenish-brown viscus sediment, which, under the microscope, was seen to be composed of many rounded masses, with minute needle-like crystals projecting from their edges. In a few instances the crystals were obtained free of the central mass and appeared as very fine needles, arranged in a radiating manner; by pressure upon the cover-slip the rosettes could be broken up into segments, each exactly resembling a half-sheath glucosazone crystal. Jolles' observation as to the thickness of the crystals was not confirmed; on the contrary, their extreme tenuity was a striking feature.

A point which must be regarded as extremely important is that repeated attempts to remove the glycuronic acid crystals by previous fermentation with yeast were uniformly unsuccessful. Solutions of glycuronic acid in water and in urine were subjected to

this procedure, with the invariable result that the acid was not removed, since subsequent treatment with phenylhydrazin always produced the characteristic crystals.

Respecting the third view, that the thornapple crystal indicates the presence of sugar, the results of experimentation given below are of interest, and seem to warrant confirmatory deductions. The writer subjected 100 different urines from apparently healthy individuals to the phenylhydrazin test with careful reference to technique; in 94 a precipitate containing yellow crystals in varying amounts was found. The 100 samples thus tested were all negative to the copper test with one exception; this reduced Haines' solution vigorously and the fermentation test showed  $3\frac{1}{2}$  per cent. of sugar; the crystals produced with phenylhydrazin were absolutely typical of sugar. In the 93 other cases the type of crystal was approximately the thornapple, appearing in completed form or in component parts, the finished crystal apparently being produced by the cleavage and spiculation of a fundamental boat-shaped crystal, with subsequent aggregation of these units into masses exactly resembling an echinoderm or "thornapple," as mentioned above.

This observation corroborates the findings of several investigators. Pavy<sup>10</sup> and Allen<sup>11</sup> secured crystals readily from healthy urine. Kisterman<sup>6</sup> in 100 specimens of normal urine found crystals of a thornapple type in every case; these as far as form was concerned could not be distinguished from the crystals of glucosazone obtained from weak aqueous solutions of sugar. Roos<sup>12</sup> examined 16 normal urines, finding crystals in each "characteristic of sugar." Frank<sup>7</sup> in all urines examined found "platelets" and "thornapple forms resembling rosettes" among the amorphous material. Moritz<sup>13</sup> found crystals in nearly every case, and Williamson<sup>3</sup> obtained a like result. Geyer<sup>14</sup> believed that a crystalline deposit could be obtained from all urines. Schilder,<sup>15</sup> by direct methods, proved that the constantly present crystals which he observed indicated sugar. MacDonald<sup>16</sup> found crystals in over one-half of all cases. Further enumeration of similar observations is scarcely necessary to establish fairly that a yellow crystalline precipitate is formed in the majority of all specimens of urine examined by the phenylhydrazin test.

Having observed the almost constant appearance of the thornapple crystals, an effort was made to discover their nature. By adding a very low percentage of grape-sugar to urine which normally gave the crystals, it was found that their number was greatly augmented; with increasing percentages a point was reached—about 0.01 per cent.—where the typical sugar crystal appeared. Further, it was found that by first subjecting the urine to thorough alcoholic fermentation the sediment was invariably amorphous. This was abundantly proven by repeated tests. Williamson<sup>3</sup> obtained precisely similar results; he regarded prolonged fermenta-

tion as essential to remove all traces of crystals on the ground that minute quantities of sugar are removed slowly with yeast. On the other hand, Geyer<sup>14</sup> obtained crystals after fermentation. It is probable that prolonged fermentation is advantageous, since it is then more apt to be complete; in the experience of the writer twenty-four to thirty hours sufficed.

In consideration of all the facts set forth in the above, the following recapitulation may be made:

1. Two forms of crystals may appear in urine after treatment with phenylhydrazin: one composed of slender needles arranged in the form of sheaves and half-sheaves is typical of sugar; the other, much smaller, composed of radiating spiculæ, aggregated into spinous masses, has been variously interpreted.

2. Glycuronic acid in urine produces a crystal very similar to the true sugar crystal. Its component filaments are very slender, and are never short and thick, as may be the case in the thornapple crystal.

3. Glycuronic acid crystals cannot be removed by previous fermentation with yeast.

4. The thornapple crystal appears in a very large proportion of all urines examined, and increases in number as low percentages of sugar are added to urine normally showing them. A point is ultimately reached in this addition where typical crystals appear.

5. Both the typical crystal and the thornapple crystal can be removed by previous fermentation with yeast.

6. It may therefore be said, in conclusion, that the small "thornapple" crystal indicates the presence of sugar, that practically all urines contain traces of sugar, and that the phenylhydrazin test will detect its presence.

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## REVIEWS.

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A TREATISE ON OBSTETRICS. FOR STUDENTS AND PRACTITIONERS.  
BY EDWARD P. DAVIS, A.M., M.D. Second edition; illustrated  
with 274 engravings and 39 plates in colors and monochrome.  
Philadelphia and New York: Lea Brothers & Co., 1904.

THE second edition of Davis' *Obstetrics* shows many important changes immensely increasing its value. The rapid appearance in the last few years of many text-books on this branch of medicine bespeaks an active generation of American obstetricians, and the product has shown great variation in scientific research, review of the literature, novelty, practical experience, literary style, and wealth of illustrations. In all these qualities the present volume reflects credit upon its publishers and its author.

In the author's preface he states that he has revised and enlarged the volume and endeavored to present concisely the latest additions to our knowledge of obstetrics which promise to be of permanent value. The work gives evidence of wide acquaintance with the recent literature of obstetrics, and the only criticism suggested is that possibly somewhat too much importance is sometimes given to the rare, the curious, and the ultrascientific; that is, if the diagnosis of the position of the placenta, the value of the *x*-ray in obstetric diagnosis, and the assistance afforded the diagnosis of pregnancy by blood and urine examination may be deemed too scientific in a text-book for students. The sixty-seven pages devoted to the physiology and pathology of the embryo and fœtus comprise an excellent résumé of the latest literature on those topics.

The chapters on the pathology of pregnancy present an interesting and practical exposition of all the important complications of pregnancy. Toxæmia and eclampsia are especially well discussed. While the author expressly states his conviction that elimination should precede operative treatment, many experienced obstetricians would not agree with his statement that "under the advantages of hospital care and with an experienced operator Cæsarean section may be considered equally with forceps or version," even when the patient is a primigravida with rigid cervix. The prophylactic and curative treatment of toxæmia is eminently practical and set forth at length and in detail. When abortion is to be induced for any grave complication of pregnancy anæsthesia and emptying of the uterus with the finger and curette is preferred to all other methods. The description of the management of normal labor is excellent;

the routine post-partum douche with bichloride solution 1:4000 is still advised. The author has very clearly stated the prevailing belief that the vagina in health requires no disinfection. Directions for the preparation for any obstetric operation through the vagina always includes the use of some antiseptic (usually lysol solution 1 per cent.). The chapter on septic infection is well illustrated with monochrome plates depicting the microscopic changes in the infected tissues. The dull irrigating curette is used to explore and disinfect the uterus. The conservatism of modern obstetrics is followed in discussing hysterectomy for puerperal sepsis. The chapters on obstetric surgery include 178 pages and details of antisepsis are described with great care. The author's experience with Cæsarean section has convinced him of its feasibility and wide application. With proper restrictions we find this operation recommended for many conditions; especially to be noted are accidental hemorrhage, face presentation with chin impacted beneath the sacral promontory, overgrowth of the foetus. Whenever rapid delivery is required in hospitals and clean private houses with an experienced operator and trained assistants the author believes Cæsarean section offers the quickest and safest method of delivery for mother and child. Symphysiotomy also has a recognized place among successful operations, its usefulness in pelvic contraction being restricted to cases where "the disproportion is not considerable, the birth canal dilated as in multiparæ, the mother and child in good condition, and the operation performed by a skilled surgeon." In the chapters upon the surgery of the puerperal state both primary and secondary repair of the cervix and pelvic floor are described and illustrated, the secondary operation being as elaborately discussed as in works on gynecology. The surgical treatment of ventral hernia and uterine displacements is also described in a separate chapter. Following an excellent and most practical chapter upon the diseases of infancy the work is concluded with an interesting discussion of the salient features of the jurisprudence of obstetrics.

R. C. N.

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LIFE INSURANCE EXAMINATIONS. A MANUAL FOR THE MEDICAL EXAMINER AND FOR ALL INTERESTED IN LIFE INSURANCE. By BRANDRETH SYMONDS, A.M., M.D., Medical Director Mutual Life Insurance Company of New York; Lecturer on Life Insurance Examinations at the University and Bellevue Hospital Medical College. New York and London: G. P. Putnam's Sons, The Knickerbocker Press, 1905.

In this interesting manual of life insurance examinations Dr. Symonds has divided the subject-matter into fifteen headings,



including two appendices, the latter being devoted to the consideration of the study of the urine and heart murmurs. Among these fifteen headings are chapters dealing with the relations of the medical examiner to the company which he serves and to the agents of the company, the examination of women, frauds and fraudulent practices, and several instructive mortality tables.

In the chapter on "Personal History of Disease" the author discusses seriatim the questions most common to the application blanks of the leading companies, and at the same time indicates the shades of meaning which the home offices require to be brought out by the examiners and the reasons therefor. There are other things than ability as diagnosticians required to make men successful life insurance examiners, and the interrelation of medicine, vital statistics, and business are most ably set forth by Dr. Symonds in this little work, which should prove a valuable guide to medical examiners throughout the country.

J. N. H.

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INTERNATIONAL CLINICS. Edited by A. O. J. KELLY, A.M., M.D., with various collaborators. Vol. IV., fourteenth series, 1905. Pp. 314. Philadelphia and London: J. B. Lippincott Company, 1905.

This volume commences with a very readable article upon the excessive use of drugs in the treatment of chronic diseases in which especial reference is made to the medicinal intoxication by Hoyem, well known for his therapeutic work. It is needless to say that the untoward events described resulted from too little knowledge of, rather than too much zeal in, therapeutics. Javal suggests a very practical point, daily weighing, in giving the indications for the dechloridation treatment of anasarca in renal diseases. The value of radium is being ascertained for the same conditions for which the Roentgen rays but a few years ago were presented, and toward a conclusion Metzenbaum gives his observations. Lejan offers an unusual but instructive article on the treatment of patients who seem desperately ill in consequence of accident, hemorrhage, or infection. In medicine, Weber and Watson present a carefully observed instance of chronic polycythemia with enlarged spleen (Vaquez's disease), which they believe to be a disease of the bone-marrow. Solis Cohen takes up the importance of pathological and of etiological diagnosis, illustrated by several instances of joint disease, in a way that tends to clarify our knowledge and to greater exactness. Duckworth has reconsidered his former ideas, and now offers his more modern remarks on the "Incidence of Gout in the United States of America," and broadens his thesis by adding "and

in new countries." Senator gives us a later word as to the clinical significance of albumosuria. The "Differential Diagnosis of the General Endowments of the Liver," by Crombie, is well written and replete with information. The "Causation and Diagnosis of Functional Heart Murmurs," by Rudolf, reviews the various theories and offers some new explanations. Surgery is well represented by papers by Bradford, Townsend, Porter, Young, Lane, Bowlby, and Gallant. In gynecology, Lockhart; in neurology, Brower; and in pathology, Warthin and Craig give full measure of instructive and well-illustrated papers. Between the ephemeral literature of the weekly and the crystallized knowledge of the text-book, the better digested knowledge of the monthly and the more elaborate paper of the quarterly have their place. This volume is well worthy of preservation for future study.

R. W. W.

APPENDICITIS: ITS HISTORY, ANATOMY, CLINICAL ETIOLOGY, PATHOLOGY, SYMPTOMATOLOGY, DIAGNOSIS, PROGNOSIS, TREATMENT, TECHNIQUE OF OPERATION, COMPLICATIONS, AND SEQUELS. By JOHN B. DEAVER, M.D., Surgeon-in-Chief to the German Hospital, Philadelphia. Third edition, thoroughly revised and enlarged, containing 64 full-page plates, 8 of which are colored. Philadelphia: P. Blakiston's Son & Co., 1905.

THE third edition of this work shows many changes and improvements over its predecessors. The portions on history and treatment have been carefully rewritten and forty-two new plates have been added, some of the older illustrations being withdrawn. Our ideas regarding appendicitis and its treatment have had to undergo so many changes in recent years that any book written four or five years ago must certainly be out of date, especially regarding treatment. The chapter dealing with the History of Appendicitis has been rewritten for this edition by Dr. Astley P. C. Ashhurst, and is most interesting. To Hancock is given the credit of the first deliberate laparotomy to open an appendicular abscess; this was done in 1848. The method did not receive general acceptance until popularized later by Willard Parker. No mention is made of the early work of T. G. Morton in this field.

The portion of the work dealing with the pathology has been rewritten by Dr. A. O. J. Kelly, and is based largely on a systematic examination of 700 appendices removed by Deaver. This portion of the subject is thoroughly dealt with.

The author's personality is recognized in the latter half of the book, which deals with the clinical aspect of appendicitis. It is interesting to note certain changes in his attitude regarding the

treatment of appendicitis. In the first place it is noticeable that although he is just as positive and forceful in his statements, he is not so dogmatic as formerly. The chapter on Symptoms is very brief, but this side of the question is elaborated in the chapters on Diagnosis. A noticeable feature is a special chapter on the Symptoms of Appendicitis in Children.

Those acquainted with Deaver's attitude in regard to prompt operation in acute appendicitis should read carefully his chapter on Chronic Appendicitis, in which he decries the reckless removal of the appendix where the symptoms are not sufficient to warrant a diagnosis. It is in the cases of chronic appendicitis that many foolish errors are made which bring discredit upon surgery, and we can heartily endorse what the author has to say. He states that "where no frank, acute attack of appendicitis has ever preceded the chronic symptoms, the surgeon will do well to decline to operate unless the physical examination shows very positively that the appendix is diseased."

A particularly instructive chapter is that on Typhoid Appendicitis, in which an interesting discussion is given of the association of typhoid fever and appendicitis. The chapter on the Blood Count in Appendicitis closes with an interesting record of the blood count after operation.

In dealing with the question of the treatment of acute appendicitis Deaver maintains his original stand that the appendix should be removed as soon as a diagnosis is made, and it must be no little satisfaction to the author to observe that most surgeons are now inclined to agree with him. Probably to no other man and to no other work can the general acceptance of this idea be more largely attributed.

The first marked change in regard to treatment is to be found in that recommended in acute appendicitis, where for certain reasons operation cannot be immediately performed. Instead of recommending saline purgatives as formerly, Deaver practically recommends the plan of treatment outlined by Ochsner, although he does not refer to this authority. He very carefully and properly, we think, shows, however, that this treatment is to be employed only under two conditions: first, where it is impossible because of circumstances to immediately operate in a case of acute appendicitis, and again in certain far-advanced cases of general purulent peritonitis in which the patient is extremely septic. In these latter cases Deaver believes that the mortality is lower where this form of treatment is employed than where immediate operation is undertaken. "But when it has become evident that the primary condition—appendicitis—is entirely overshadowed by the secondary condition—peritonitis—and that any operation will only hasten the fatal termination, then I think that a form of treatment based upon the withdrawal of food by mouth, the substitution of nutrient

enemas and hypodermic stimulation, is the only one which gives these patients even a fighting chance for recovery." If the process quiets down and abscesses form, these can be drained and the appendix removed later. He heartily approves of a statement of Murphy, that the extent of the operation in certain cases of abscess and of peritonitis must be governed by the constitutional symptoms of sepsis which the patient presents. Here again is a noticeable change from the author's previous attitude, where he recommended the removal of the appendix in every case. He is particular to advise that surgeons of limited experience should not feel themselves obliged always to remove the appendix at the primary operation in cases of abscess or of peritonitis.

Of all the incisions which have been recommended for opening the abdomen in cases of appendicitis, Deaver prefers that through the right rectus muscle. In cases of diffuse peritonitis the author no longer practises irrigation, but prefers to do as little manipulation as possible, instituting drainage and placing the patient in the semisitting posture, a form of treatment which has been so strongly urged by Murphy.

The latter portion of the book consists in a description of the complications and sequelæ of appendicitis. As a practical guide to the diagnosis and treatment of appendicitis, we think this work is particularly reliable.

The book itself is very light considering its size, and the illustrations are quite satisfactory. We do, however, think it is a mistake in a book of reference to have uncut leaves. In a book to be read but once this is excusable, but in one which is apt to be constantly referred to smooth edges are a great deal more convenient.

J. H. G. }

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#### THE MEDICAL EPITOME SERIES. DISEASES OF THE EYE AND EAR.

A MANUAL FOR STUDENTS AND PRACTITIONERS. By ARTHUR N. ALLING, M.D., Clinical Professor of Ophthalmology in the Yale University, Department of Medicine, New Haven, Connecticut, and OVIDUS ARTHUR GRIFFIN, B.S., M.D., late Demonstrator of Ophthalmology and Otology, University of Michigan, and Oculist and Aurist, University Hospital, Ann Harbor, Michigan. Series edited by VICTOR COX PEDERSEN, A.M., M.D., Instructor in Surgery and Anæsthetist and Instructor in Anæsthesia at the New York Polyclinic Medical School and Hospital; Genito-urinary Surgeon to the Out-patient Departments of the New York and the Hudson Street Hospitals; Anæsthetist to the Roosevelt Hospital. Philadelphia and New York: Lea Brothers & Co.

THIS epitome answers the purpose for which it is intended. The questions appended to each chapter make it a good quiz compend to

refresh the student's memory. And while it is not expected that the physician's library shall contain no other works upon the subjects of which it treats, it will prove of service in furnishing a compact reference book for the busy practitioner. The numerous illustrations, which are not so commonly found in books of this class, add to the value of the text. T. B. S.

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A COMPEND OF DISEASES OF CHILDREN. ESPECIALLY ADAPTED FOR THE USE OF MEDICAL STUDENTS. By MARCUS P. HATFIELD, A.M., M.D., Emeritus Professor of Diseases of Children, N. W. U. Medical School; Physician to Wesley Hospital, etc. Third edition, thoroughly revised, with a colored plate. Philadelphia: P. Blakiston's Son & Co.

THIS little book is already well known as one of the popular series of Blakiston's "Quiz Compends." The present edition has been thoroughly revised and brought down to date, and an appendix of 13 pages is largely devoted to additions on the subjects of milk supply and infant feeding. In the 235 pages of closely printed text Dr. Hatfield has presented the subject concisely and for the purpose adequately. The style is terse and readable, and the classic arrangement enables the student to gain a very satisfactory understanding of the subject in the brief time that can be allotted to a branch that usually receives scant attention in the average medical curriculum. The frontispiece gives an excellent diagram in appropriate colors of the fetal circulation. T. S. W.

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EXAMINATION OF THE URINE: A MANUAL FOR STUDENTS AND PRACTITIONERS. By G. A. DE SANTOS SAXE, M.D., Assistant Pathologist to the Columbus Hospital, New York; Member of the American Urological Association, etc. Fully illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1904.

As a guide to the routine examination of urine, one will find this small book of use, though it is not stamped with a striking individuality. In great part the manual is a compilation of the larger text-books from which material most useful for practical urine examinations has been gathered. The subject is treated in the usual manner, and all the well-known and generally accepted methods of urine analysis are described. At the end of each chapter a series of questions is added to help the student in review. The book is divided into four parts. Part I. contains the introductory

chapters and deals with general considerations of the urine as a secretion, its physical properties, etc.; Part II. is devoted to the "Chemical Examination of the Urine;" Part III. to the "Microscopic Examination;" and Part IV. to the "Diagnosis of Urinary diseases." Although Part IV. contains valuable information, still the subject is treated in rather a didactic manner.

The book is attractively bound in soft leather, well printed, and well illustrated.

W. T. L.

ERRORS OF REFRACTION AND THEIR TREATMENT: A CLINICAL POCKET-BOOK FOR PRACTITIONERS AND STUDENTS. By CHARLES BLAIR, M.D., Fellow of the Royal College of Surgeons of England; Surgeon to the Western Ophthalmic Hospital, London; Ophthalmic Surgeon to the Royal Hospital, Richmond. Bristol: John Wright & Co. London: Simpkin, Marshall, Hamilton, Kent & Co., Ltd., 1905.

THE subject is necessarily compressed in this pocket-book of a hundred pages. We doubt if it will be of much use "to some who are not able to give much time to this relatively uninteresting subject," as the author hopes. It may find a place in the hands of students who are under instruction, and thus prepared to comprehend a syllabus, for it is little more, of the subject of refraction and accommodation and their anomalies.

The explanations and practical directions are in the main in accordance with present-day conceptions. We note, however, some adhesion to older methods which have been improved upon; for example, the shadow test is described with a concave mirror, and nothing is said about the superiority of the plane mirror with the light not over the patient's head but close to the observer. The author also is a firm believer in the necessity of making some considerable deduction in ordering convex lenses for hypermetropia from what he considers the full correction, to allow for "a certain natural tonic contraction of the ciliary muscle, which is always present except when a mydriatic has been used." In an example given in this connection where +4 was found by the shadow test, and confirmed subjectively, it is recommended that +3 be ordered. We do not believe that such a contraction exists except in exceptional cases. The difficulty here is that the so-called full correction is not the true correction; that is, the lens given by the subjective tests adapts the eye for the distance at which the patient is placed from the test card, rendering him myopic to that extent if convex lenses are used, or leaving a slight degree of myopia if the lenses be concave. In either case the proper allowance for the range is necessary to adapt the eye for infinity. We

are convinced that the neglect of taking this fact into consideration is responsible for the belief in the constant existence of a tonic contraction of the ciliary muscle. Such contraction is occasionally, but comparatively rarely met with as a spasm of accommodation.

In the correction of presbyopia the author gives proper weight to the fact that not all of the accommodative power can be employed for continuous near work, but that one-third must be kept in reserve. He also well observes that the patient's age "should guide but not determine" the strength of glass to be prescribed.

The style of this little book is very clear, making its perusal easy and agreeable.

T. B. S.

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KLINIK DER VERDAUUNGSKRANKHEITEN. By DR. C. A. EWALD.  
Volume III. Diseases of the Intestine and Peritoneum. With  
75 illustrations. Berlin: August Hirschwald.

THIS excellent little book consists of a series of lectures upon the diseases of the intestines. After a careful description of the methods of investigation, including that most difficult and unsatisfactory branch of laboratory diagnosis, the examination of the feces, Ewald discusses nutrition, particularly its effect upon the activity of the intestines, and, as a natural sequel to this, the treatment of constipation. In this he depends more upon a general hygienic and dietetic treatment than upon either the physical or drug methods. The following lectures are devoted to inflammation and ulceration of the intestinal tract, including appendicitis, to the discussion of which he devotes a very considerable amount of space. In accordance with the rather prevailing German sentiment on this subject, Ewald is conservative regarding operation. He believes that it is indicated only in four conditions: First, if there is perforation with general peritonitis, when it should be done as soon as possible; second, when there is definite evidence of an accumulation of pus, and the course is progressive; third, when there are frequent relapses; and, fourth, when there is chronic appendicular colic, and the larval form of appendicitis with indefinite symptoms. Of course, the opinion of American surgeons would strongly oppose the restriction of the operation to these few conditions.

The lecture upon tumors of the intestinal tract is rather more summary in character than the importance of this subject demands. The differential diagnosis is treated in an entirely inadequate manner. The same may be said of the diagnosis and treatment of intestinal obstruction. For the latter condition he considers opium the most valuable internal medicament.

The final chapters deal with diseases of the rectum, the nervous

diseases of the intestine, parasites, and the diseases of the peritoneum. The book is sparingly illustrated, but the illustrations are clear and well selected; many of them are original. It lacks a table of contents, but has an excellent index. It may be regarded as one of the essential text-books upon the subject of which it treats.

J. S.

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A NON-SURGICAL TREATISE ON DISEASES OF THE PROSTATE GLAND AND ADNEXA. By GEORGE WHITFIELD OVERALL, A.B., M.D., formerly Professor of Physiology in the Memphis Hospital Medical College. Chicago: Marsh & Grant Co.

IN this small volume the author describes the great benefits to be derived from the various forms of electricity in the treatment of diseases of the prostate. His remarks are illustrated by reports of many cases. The unqualified abuse of the various operative procedures, especially for prostatic hypertrophy and the unwarrantedly low estimate of the results accomplished by these, inclines one to put less confidence in the results which the author claims for his own non-surgical methods. He also shows too great a tendency to refer to the previous unsuccessful treatment of his own patients at the hands of "prominent genitourinary specialists." Much of his space is taken up in describing the evil results of operations upon the prostate and extremely little in the dangers and failures of electricity. It is noticeable also that his references to the operative treatment of prostatic hypertrophy has to do with those operations which were in vogue some ten years ago. His quotations from surgeons regarding the dangers and mortality of prostatectomy are somewhat misleading, as the context is in most instances omitted, causing the remarks quoted to convey quite a different meaning from that intended by the writer. It is undoubtedly true that all cases of prostatic disease or hypertrophy do not require a surgical operation, and it is equally true that electricity is by no means applicable to all, as the writer would have us believe.

The following quotation is a type of many paragraphs in this small volume: "Hypertrophic prostatic diseases, owing to their intractability, have been made, by the ambitious surgeon, the object of many operative procedures, each of which challenges its predecessor in the endless suffering entailed upon its victims, or in its lethal dangers supplying topic for lengthy discourses upon the superior claims of each operation as revealed by the *autopsy*."

We believe that the author has, in this book, greatly overestimated the non-surgical treatment of diseases of the prostate, and we know that he has grossly underestimated the results of the surgical treatment.

J. H. G.



THE PRACTICAL MEDICINE SERIES OF YEAR BOOKS. Comprising ten volumes on the year's progress in Medicine and Surgery. Under the general editorial charge of GUSTAVUS P. HEAD, M.D., Professor of Laryngology and Rhinology, Chicago Post-graduate Medical School. Volume I. General Medicine. Edited by FRANK S. BILLINGS, M.S., M.D., Head of Medical Department and Dean of the Faculty of Rush Medical College, Chicago, and J. H. SALISBURY, M.D., Professor of Medicine, Chicago Clinical School. Series 1905. Chicago: The Year Book Publishers.

WITH this volume, the first for the current year, a review of general medicine is presented. The subject of tuberculosis is given the most important place and more space is devoted to that disease than to any other in the text. The latest theories of its causes, exciting and predisposing; the diagnosis and treatment, including the use of tuberculin, are discussed quite freely considering the size and scope of the work. Among other topics of general medicine considerable attention is given to the diseases of the blood and blood-vascular system and the kidneys. Most of the three hundred and odd pages are occupied with the above-mentioned subjects; there are short sections on the infectious, parasitic, and metabolic diseases, while a few pages are devoted to the diseases of the ductless glands. The book, like the others of the series, affords an easy method of keeping up to date in medical literature, and is superior to some of its predecessors in the clearness and lucidity of the text. .

A. N.

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THE INTESTINAL CATARRHS: BEING A CLINICAL STUDY OF COLITIS, APPENDICITIS, AND THEIR ALLIES, WITH A SPECIAL NEW SECTION ON SPRUE. By EDWARD BLAKE, M.D. Second edition. Chicago: W. T. Keener & Co. London: H. J. Glaisher.

THIS book is a genuine new edition, more than double its former size, of the author's work on colitis published in 1904, with added sections on Sprue and Treatment. The book is divided into twelve sections, each having attached a full bibliography. We find in this work an extremely interesting and original presentation of a very little understood subject. It is a further contribution to the author's scientific and philosophic plan of accumulating data for the synthesis of disease. Perhaps like all pioneers he has become so impressed with the importance of these very useful observations that he is inclined to overestimate their significance. However, the reader must bring his critical faculties to bear and interpret the author in the light of his own experience.

J. B. S.

# PROGRESS OF MEDICAL SCIENCE.

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## MEDICINE.

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UNDER THE CHARGE OF

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**Sugar Metabolism and the Combustion of Carbohydrates in the Muscles.**  
—More than a year ago PROF. OTTO COHNHEIM (*Zeitschrift für Physiologische Chemie*, Band xxxix., p. 336) published the results of experimental researches which seem to afford the most satisfactory explanation for the manner in which the carbohydrates are normally warehoused in the body. By means of a specially constructed press he obtained quantities of juice from the pancreas and muscles of cats and dogs. With each of these he first experimented separately. The juice of the pancreas when added to a solution of glucose was inactive. So also was the muscle juice when used in the same way. On first mixing the juices of the pancreas and muscles together, however, and then adding the mixture to solutions of glucose, there was a rapid and eventually a complete conversion of the latter into alcohol and carbonic acid. Cohnheim holds that the ingested carbohydrates are burnt up mainly in the muscles. He gives two possible explanations for the remarkable result noted above. One is based on Ehrlich's side-chain theory. According to this view, the pancreas and muscles provide complementary and intermediate bodies, both of which are necessary for normal carbohydrate metabolism. His second explanation is in accord with Pavlov's findings regarding the relationship between trypsinogen, the proteid enzyme of the pancreas, and proteid digestion. Pavlov found that trypsinogen itself was inactive on proteids, but when it came into contact with the "enterokinase" of the intestinal juice it was converted into trypsin and then caused rapid digestion of proteids. Cohnheim believes that both the muscles and pancreas produce enzymes which are necessary for carbohydrate metabolism. That of the muscles is probably a proenzyme and requires the action of the ferment produced by the pancreas and contained in its internal secretion before it can become active on carbohydrates. This important work has a direct bearing on the etiology of diabetes mellitus. In this disease, in many

of the cases at least, the enzyme of the pancreas or muscles is believed to be lacking. The circulating glucose is accordingly not burnt up in the muscles, a hyperglycæmia occurs, and the excess over physiological limits begins to be excreted in the urine. The investigations in recent years on the relationship between degeneration of the islands of Langerhans and diabetes mellitus seem to indicate that in many cases the pancreatic enzyme is probably lacking in this disease.

Cohnheim proceeded to ascertain the characteristics of these bodies which he at first thought to be ferments. Recently (*Zeitschrift für Physiologische Chemie*, Band xlii., p. 401) he published the results of his study of the characteristics of the glycolytic body of the pancreas. He finds that it withstands boiling, is soluble in water and 96 per cent. alcohol, but is insoluble in ether. For these reasons he believes that the glycolytic agent of the pancreas is really not a ferment, but a body very closely allied in its characteristics to such other well-known constituents of internal secretions as adrenalin, iodothylin, and secretin. An interesting feature is that an excess of this body hinders, and when present in large quantities, absolutely prevents carbohydrate combustion. The most active sugar destruction occurs when muscle and pancreas are mixed together in the proportion of 75 grams of the former to 0.8 grams of the latter. When more than 0.8 grams of pancreas are added the activity diminishes and ceases when 2 grams are reached.

Cohnheim suggests two explanations for this remarkable finding. The first is that the pancreas produces two substances, one of which favors and the other hinders sugar combustion. For various reasons he sets this aside as a possible explanation. The second explanation is based on the observation of Neisser and Wechsberg that the destruction of bacteria by a bactericidal serum is due to the combined action of amboceptors and complements, and that an excess of amboceptors destroys the bactericidal action of the serum. By analogy, he suggests that by adding an excess of pancreas juice to a mixture of sugar solution and muscle juice an overabundance of amboceptors is provided, thus destroying the glycolytic action of the two juices.

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**The Urinary Sugars of the Pregnant, Parturient, and Lactating Woman.**  
 —COMMANDEUR and PORCHER (*Archives générales de médecine*, September 6, 1904, p. 2241, and September 13, 1904, p. 2305) report the results of the urinary examinations of 31 pregnant women whom they have followed with especial care. After giving in detail the physiology of mammary secretion, the technique in their investigations, the historical review of the urinary sugars, and the report of their individual cases, they cite their conclusions which may be briefly summarized as follows: "Ante-partum" lactosuria is constantly present in the last weeks of pregnancy. Negative reports are due to faulty technique. It may be considered as a physiological condition. The lactose of the mammary secretion is formed from the glucose of the circulating blood. The lactosuria results from the development of activity in the mammary gland and is dependent on the hypertonicity of the mammary secretion. Lactose passes into the general circulation and is eliminated by the kidneys. The amount in the urine is usually about 1 gram to the litre. It may reach 2 grams, but rarely more.

"Ante-partum" glycosuria is of two forms. Pregnancy may occur in a person with true diabetes. Here all the usual diabetic manifesta-

tions may be present. The child rarely lives to full term and the mother very frequently dies of diabetic coma shortly after delivery. The second form is a very mild type. No symptoms are referable to the condition. The only change in the urine is the existence of a small amount of glucose which does not increase its specific gravity. The writers regard this glycosuria as physiological. According to their view the liver throws an excess of glucose into the circulation in the late weeks of pregnancy, and where the breasts fail to convert all the excess into lactose a certain amount is eliminated by the kidneys. This glycosuria is constantly accompanied by a lactosuria. It occurs equally in primipara and multipara, and increases in grade up to full term, when it disappears and gives place to lactosuria alone. This form seems to have no bad influence on pregnancy whatever.

"Post-partum" lactosuria is more marked than the ante-partum. It is dependent on the activity of the mammary gland and also on a certain degree of stasis. This stasis may be due merely to the fact that the gland secretes more milk than the child requires in the first few days after birth. The maximum grade of the lactosuria is reached from the third to the fifth day after labor. The amount of lactose varies between 1 and 8 grams to the litre.

The writers observed no cases of "lactation" lactosuria, that is, where lactosuria occurs later during the period of lactation. It exists, however. It may occur if, for any reason, the child fails to take the breast properly; also if there be any obstruction of the milk ducts and occasionally in abscess of the breast.

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**The X-ray Treatment of Leukæmia.**—LEDINGHAM and McKERRON (*The Lancet*, January 14, 1905, p. 71) report a case of myelogenous leukæmia remarkably improved by treatment with  $\alpha$ -rays. The patient was a boy, aged eleven years. The spleen reached to within a finger's breadth of the pubes. At the onset of the treatment on May 17, 1904, the red cells were 3,300,000 and the leukocytes 220,000 per cmm. The  $\alpha$ -rays were administered on alternate days for from ten to twenty minutes. They were applied over the splenic tumor, the lower epiphyses of the femora, and occasionally over the vertebræ and sternum. By July 5th, or in a space of six weeks, the leukocytes fell to 23,000. From this date to August 15th, when the treatment was stopped, they failed to further diminish in numbers. Before the treatment began the myelocytes exceeded the polymorphonuclears, but when it was stopped they were much fewer but were still present. The red cells rose to 5,000,000. The spleen in their case failed to diminish materially in size.

The writers were led to give the treatment a trial owing to the successful treatment of a case by Senn and of 2 cases by Bryant and Crane. In all three instances the absolute numbers and relative percentages of the leukocytes returned to normal. The myelocytes entirely disappeared. They review the literature and give abstracts of the recorded cases. With one or two exceptions all the cases treated with the  $\alpha$ -rays have experienced a remarkable improvement in both the objective and subjective symptoms. The red cells increase rapidly toward normal. The effect on the leukocytes is similar to that of an acute infection. In a number of the cases they have returned to normal and the myelocytes have disappeared. In many cases the spleen has markedly reduced in size. The writers think that when the spleen has become

fibrosed in prolonged cases of leukæmia no material reduction in its size can be expected. The results of the treatment in lymphatic leukæmia have not been quite so satisfactory, although marked benefit has been recorded in some instances. The glandular enlargements in this form as well as in Hodgkin's disease occasionally show marked diminution in size. The writers think that the experience is still too limited to fairly estimate the true value of this new treatment. They say: "When these so-called 'cured' cases and those in which marked improvement has resulted have been under observation for some considerable time, with or without renewal of the treatment, we shall be in a better position to judge of the true value of this novel therapeutic method."

Various theories for the beneficial effect of the  $x$ -rays in leukæmia have been advanced. Senn attributed it to their antiparasitic action on Lowit's "*hæmamœba leukæmia*." The actual existence of this organism is strongly doubted. According to the experimental work of Mosse and Milchner the rays cause actual destruction of the white elements of the bone-marrow while the red cells, nucleated and non-nucleated, are unaffected. According to Ehrlich there is an enzyme in myelæmia which has a positive chemotactic influence on the white elements, calling them out into the circulation. Lepine and Boulad have shown that the  $x$ -rays destroy enzymes and this may be the explanation of the beneficial results in leukæmia.

**Investigation of the Stomach Contents in Old Age.**—SEIDELIN (*Berl. klin. Wochenschrift*, 1904, xli. p. 945) investigated the stomach contents in 70 persons over the age of fifty years. The subjects were hospital patients with various chronic ailments and cannot, therefore, be accepted as representing a perfectly normal standard, even though all cases of gastric disease were carefully excluded. Ewald's test breakfast was used. The total acidity, free hydrochloric acid, combined acid and peptogenic power of the gastric juice were determined. One patient received only one test meal, but in all others from two to four at least were given. None of the cases in the series gave a reaction for lactic acid. Special importance is laid on the reaction for free hydrochloric acid. The percentages are given in round numbers.

Of the 70 cases, 28, or 40 per cent., showed a constant absence of free hydrochloric acid. In some of these cases the acidity was so low as to suggest an achylia gastrica, but in none was the peptogenic power absent. In only 6 cases (10 per cent.) was the free hydrochloric acid constantly within normal limits. In 7 there was uniform hyperchlorhydria; in 7 constant hypochlorhydria, while in 22 the free acid value varied so widely that they could not be classified. Of 57 patients without gastric symptoms, free hydrochloric acid was absent in 24. Arranged according to age, we have the following:

Patients from fifty to fifty-nine years, 22 cases, 10 with achlorhydria, 45 per cent. Patients from sixty to sixty-nine years, 23 cases, 9 with achlorhydria, 39 per cent. Patients from seventy to seventy-nine years, 15 cases, 6 with achlorhydria, 40 per cent. Patients from eighty to eighty-nine years, 10 cases, 3 with achlorhydria, 31 per cent.

These figures would indicate that advancing age is not an important factor in the occurrence of achlorhydria, but, of course, they must be accepted with caution.

Chronic constipation was present in 43 cases, of which 13, or 30 per cent., were without free acid. This percentage is not as high as that for all 70 cases, and may bear some relation to the fact that, as Faber has shown, chronic constipation is usually accompanied by an increased acid secretion. Five of the 7 cases with hyperchlorhydria suffered from chronic constipation. Of 16 cases with a history of chronic alcoholism free hydrochloric acid was absent in 7, a percentage very little above that for the whole series. There was clinical evidence of arteriosclerosis in 48 cases; 24 of these were without free hydrochloric acid. In the remaining group of 22 cases without arteriosclerosis, there was achlorhydria in only 4. Cases of hypochlorhydria and hyperchlorhydria occur, however, in both groups, and the cases of hypochlorhydria are not more numerous in the first than in the second. The influence of arteriosclerosis appears more marked in cases from fifty to fifty-nine years of age, and least marked in those from eighty to eighty-nine years, suggesting that the early, abnormal arterial changes are of more moment in influencing the gastric secretion than those which normally occur in later years. These results demonstrate that the stomach secretion may be preserved unchanged in advanced age, but the unusually large number of cases without free hydrochloric acid should put us on our guard in attributing diagnostic importance to its absence.

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## SURGERY.

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UNDER THE CHARGE OF

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**An Unusual Case of Diaphragmatic Hernia.**—NEWHAM (*The Lancet*, December 24, 1904) reports the case of a man who was brought to the hospital with the history of having sustained a fall of about 30 feet. On admission he was found to have sustained a fracture of the left femur and considerable bruising of the chest and abdomen, but there was no evidence of any fracture of the ribs. He was vomiting and in a generally collapsed condition. On examination of the abdomen some dulness was made out in the flanks, which shifted on moving the patient. The diagnosis of probably ruptured spleen was made, but, owing to the generally grave condition of the patient, operative interference was out of the question. The patient was placed in bed and on medical treatment, and made favorable progress until his discharge two months later, except for attacks of pain over the cardiac region, somewhat increased on taking his food, which consisted of milk, bread and butter, and milk pudding. After leaving the hospital he still

complained of these attacks of pain, which were not accompanied by vomiting. The attacks persisted and about two months after being discharged from the hospital he was suddenly seized with a violently severe pain, accompanied by vomiting, which did not respond to medical treatment and which was followed by death in the course of two days. The autopsy showed the fracture in the femur, but there was no evidence of any fracture of the ribs. On removing the chest wall the first organ to present itself to view was the stomach, accompanied by part of the transverse colon, both greatly distended and the latter showing signs of strangulation. These practically filled the left side of the thorax, except for about ten ounces of blood-stained fluid which were present. The left lung was firmly pressed back against the spinal column; it was quite airless, small, and deeply pigmented. The heart was healthy, though small, and pushed over well to the right of the sternum. The right lung was completely bound down by pleuritic adhesions and was with difficulty removed from the body. The left lung was rather smaller than usual and somewhat congested. On examination of the diaphragm an opening slightly to the left of the middle line, with smooth edges, and easily admitting the index-finger, was found through which the stomach and intestines had escaped into the thoracic cavity. The liver was of average size and healthy, but somewhat more to the right side than usual. All the other organs were healthy. The hole in the diaphragm appears undoubtedly to have been made at the time of the accident and was probably caused by sudden violent muscular contraction. It seems, however, almost incredible that such a large hernia, which must have existed for some time to produce such pressure symptoms, could be compatible with life.

**On Duodenal Ulcer, with Notes of Fifty-two Operations.**—MOYNIHAN (*Lancet*, February 11, 1905), from January, 1900, to September, 1904, operated on 52 cases. There were 7 perforating duodenal ulcers, with 5 recoveries; 22 operations for duodenal ulcers associated with gastric ulcer, with 1 death, and 23 operations for duodenal ulcer alone, with 1 death.

The relative frequency of duodenal ulcer to gastric ulcer has been greater in his experience than in many of the statistics published by others, but the discrepancy, he thinks, is easily accounted for by the fact that the statistics quoted in the text-books are based exclusively on post-mortem examinations, while his investigations have been confined to the living.

Moynihan considers that duodenal ulcer is far more frequent than has been formerly believed, and that the association of duodenal ulcer with gastric ulcer is frequent. The text-book statement concerning the difficulty in diagnosis may explain its apparent infrequency. He believes that the symptoms in many cases are perfectly characteristic and admit of an unhesitating diagnosis. On the other hand, he says that in some cases the diagnosis is impossible, because gastric ulcer and gall-bladder disease may both be complications in the same case.

Generally duodenal ulcer is in the first part of the duodenum, at least ten times more frequently than in the second portion, which is the next most frequent situation of the ulcer.

In about 50 per cent. of duodenal ulcers gastric ulcer is associated, the frequent association of the two being due to the fact that with peptic

ulcer there is a marked increase of the hydrochloric acid, which, when the contents of the stomach empties into the duodenum, causes a peptic ulcer of that part of the wall with which it comes in contact, the sequence of events being gastric ulcer, hyperchlorhydria, duodenal ulcer.

Surgical work on the stomach has established the fact that ulcer of the stomach and duodenum are frequently multiple. The text-books say that gastric ulcer is usually solitary. The reverse is the fact. Duodenal ulcer may occur at any age. It has been found as early as the third and fourth day, and even as early as the time of birth. It is usually said that duodenal ulcer occurs much more frequently in the female. Moynihan found, in his 51 cases, 32 in males and 19 in females.

The symptoms are pain, hæmatemesis, and melæna. In certain cases, 20 per cent. according to Morot, the ulcer is latent, and is revealed only by perforation or hemorrhage. Pain when severe is always worse to the right of the median line. If the pain comes on two to four hours after a meal, the ulcer is surely at or near the pylorus. The pain in such circumstances Moynihan calls "hunger pain," that is, it comes on when the patient begins to feel that another meal is due. The cause of the pain is not known. It may be different in different cases, or in the same patient at different times. The more likely causes are irritation of the open ulcer by the acid gastric contents, pyloric spasm, distention of the stomach or duodenum, or both, by gas, and the occurrence of a localized peritonitis. The relief from pain following the taking of food is due, it is suggested, either to the closure of the pylorus, caused by the irritant action of the fluid, or to the dilution of the excess of free hydrochloric acid.

Hæmatemesis and melæna may be present together, or either in the absence of the other. The presence of blood by the bowel is probably more frequent than Moynihan's statistics show. In 23 cases of duodenal ulcer alone, hæmatemesis and melæna were observed in 4 cases, hæmatemesis alone in 3 cases, and melæna alone in 2 cases. The presence of moderate or even large quantities of blood in the stools is more likely to be overlooked than small quantities in the vomit.

Hemorrhage from a duodenal ulcer is more persistent, probably less easy to check, and undoubtedly more insidious than hemorrhage from a gastric ulcer. Operation to check it is, therefore, more imperative.

Moynihan performed gastroenterostomy alone in all his cases, and in all the hemorrhage ceased at once. There are cases in which excision of the ulcer, if easily accomplished, would be desirable; and there may be cases in which ligature of a large vessel in the ulcer would be necessary. Gastroenterostomy must be performed whether the ulcer is treated separately or not, in order to give rest to the duodenum.

Perforation is more likely to occur in duodenal than in gastric ulcer, and its consequences are more disastrous. The remarkable mimicry of appendicitis is due to the direction which the extravasated fluid takes, down the hillock to the right of the transverse colon, down the ascending colon to the iliac fossa. In 51 cases of perforation from duodenal ulcer collected by Moynihan, 19 had been operated on after an erroneous diagnosis of appendicitis had been made.

In 10 of the 51 cases of duodenal ulcer reported in this paper, there was obvious evidence of disease of the gall-bladder, or bile-ducts with or without gallstones. The disease in the duodenum may be primary and that in the gall-bladder secondary; the reverse may be true, or both



may be entirely independent. In 1 case the gall-bladder contained a single large stone which had ulcerated through the duodenum, which it blocked.

Duodenal ulcer may be mistaken for cholelithiasis. In both the pain may be colicky or persistent, and may radiate in the same direction, and in both there is an excess of free hydrochloric acid. As Moynihan found them, there was little or no difficulty in diagnosis. In both surgical treatment offers the speediest and safest relief.

The association of pancreatic disease with duodenal ulcer has received very little attention. It was present in 3 of the 51 cases. The deepening ulcer may reach the pancreas, which then forms the basis of the ulcer, and is involved in the inflammatory process. A condition of chronic pancreatitis may be present from the same causes which gave rise to the duodenal ulcer—alcohol, for example, or perhaps syphilis.

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**Septic Origin of Gastric and Duodenal Ulcers.**—CLARKE (*Lancet*, February 11, 1905) reports a case of a sailor who suffered from an ulcer in the region of the pylorus, extending both toward the stomach and duodenum, which had its origin six years before during a shipwreck. The patient spent sixteen days in an open boat, and during that time suffered greatly from exposure, and had nothing to eat but some mouldy bread. The water he drank was putrid. Two days after he was rescued he suffered from violent pains in the stomach and vomited everything he ate for five days. He was never well from that time.

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**Richter's Hernia.**—LOWE (*Lancet*, January 28, 1905) reports 4 cases of this variety of strangulated hernia observed recently in the wards of St. Mary's Hospital. The diagnosis is not always easy, and for this reason it is constantly overlooked in its earlier stages. Consequently its mortality is high. It is not so rare as previously thought. There were several other cases in the wards of this hospital during the last year, in addition to the 4 under the writer's care. Treves' paper (1886) still remains the best summary in connection with this condition. It occurs more frequently in women and in femoral hernia, and is found only in adults. The bowels may be opened during the whole process of strangulation or may act occasionally, and will often respond to aperients.

The first and last of the cases illustrate two of the chief difficulties with regard to determining accurately the nature of these cases.

In connection with the first case, it is noted that in the previous September a similar attack was ascribed to inflammation of a crural gland, and in the earlier stages of the final attack the same diagnosis was made.

In the last case there was no question as to the hernia, but six days after it had become larger and more tense, the woman had none of the appearances of a case of strangulated hernia, and the condition might have been mistaken for an inflamed sac or an obstructed hernia. This emphasizes the necessity of cutting down on any hernia that has become suddenly larger and is irreducible.

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**A Second Case of Cutaneous Anthrax Successfully Treated by Sclavo's Serum without Excision.**—BOWLBY and ANDREWS (*British Medical Journal*, February 11, 1905) report a case of a man, aged thirty years, a hairdresser, who, on January 9th, bruised his forehead without breaking the skin. Four days afterward some watery fluid

exuded, and on the fifth day a small black slough appeared, and the neck became stiff. On the sixth day an enlarged gland appeared at the left angle of the jaw. His general health was scarcely impaired, and there was little pain. On admission to St. Bartholomew's Hospital, on the eighth day, the black spot was the size of a sixpence, and there was a ring of vesicles around it, but not much inflammation. The temperature was  $99.6^{\circ}$  and the pulse 100. The fluid from the vesicles showed practically pure cultures of the anthrax bacillus. The sole treatment consisted of the injection under the skin on the day of admission of 40 c.c. of Sclavo's serum. No rise of temperature followed. Next day the pulse was 76, and there were no constitutional symptoms. There was less local discomfort, and the gland at the angle of the jaw had decreased in size. The œdema, however, had increased, and on the following day had still further enlarged, but with no increase in the size of the slough and no fresh vesicles. The gland continued to diminish, and then the œdema, until by January 21st it was all gone. Convalescence was uninterrupted, and the slough separated January 31st, fourteen days after the administration of the serum.

The anthrax bacilli were abundant on the day of admission to the hospital. On the following day, nineteen hours after the injection of the serum, by precisely the same methods of examination, no anthrax bacilli could be found in the fluid from the vesicles. Later examinations were equally negative.

The increase of œdema after injecting Sclavo's serum was noted in the first case also. It is suggested that it is due to the liberation of an intracellular toxin from the disintegrated bodies of the bacilli, some of which were observed in the discharge from the vesicles.

These results seem to indicate that, at least in moderately early cases of cutaneous anthrax, excision may safely be dispensed with, where an initial dose of 40 c.c. of the serum is employed.

**Arteriovenous Aneurysm of the Internal Carotid and the Cavernous Sinus following a Fracture of the Base of the Cranium.**—HANNECART and LABARRE (*Journal de chirurgie et annales de la société belge de chirurgie*, February, 1905) state that the presence of the aneurysm was suspected soon after the accident and before any objective signs were detected. This was based chiefly upon a sensation perceived by the patient, within the cranium, like the "sound of a locomotive." One month later there appeared a dilated network of veins in the sclera, exophthalmos, and the intracranial soufflé was perceptible on auscultation. From that time all these symptoms progressively increased.

The dilatation of the ciliary veins indicates a disturbance of the circulation in the ophthalmic vein, which empties into the cavernous sinus. Obstruction to the current in the sinus leads to congestion of the ophthalmic veins and its tributaries, consequently of the ciliary veins. The exophthalmos is due to the same cause and is pulsating.

The lesion is accounted for by the apparent course of the line of fracture along the middle fossa and through the sphenoid bone, thus crossing the course of the sigmoid sinus and internal or carotid artery.

The treatment may be expectant, but this would not remove the intracranial soufflé, and would risk a fatal termination from rupture of the aneurysm. M. Gallemaerts cured a similar case by constant pressure over the eye with a bandage, and intermittent compression of the prim-

itive carotid carried out by the patient himself. Ligation of the carotid might cause the souffle and the exophthalmos to disappear, but, on the other hand, it might interfere with the cerebral nutrition. The writers were still undecided as to what course they would pursue.

**The Rectal Touch as a Means of Diagnosis and Treatment in Acute Blennorrhagic Urethritis.**—LEBRETON (*Annales des maladies des organes genitourinaires*, March 15, 1905) states that blennorrhagia very frequently invades the posterior urethra and is often very precocious. As a therapeutic measure, massage, or, according to Guépin, prostatic expression, empties the glandular crypts of all the pathological products which have accumulated in them. It thus prevents the formation of pus pockets, in the depth of which the gonococci, at their leisure, develop their virulence.

Whenever the pressure of the finger gives no pain in the region of the prostate, it is useless and even dangerous to practice massage, since it will only irritate the organ, rendering it more vulnerable to infection, which is always possible.

## THERAPEUTICS.

UNDER THE CHARGE OF

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**The Copper Treatment of Water.**—PROF. HENRY KRAEMER has performed a series of experiments for testing the efficiency of copper in reducing the number of micro-organisms in drinking-water. Those competent to pronounce upon the matter concur in the belief that the use of copper is the only practicable and efficient means of removing *algæ* from the water of streams and reservoirs without affecting higher plant or animal life. Why, then, should not the same substance have its sphere of usefulness in rendering water contaminated with pathogenic organisms fit for drinking? While poisoning from copper is a possibility, authorities state that this metal, while toxic to micro-organisms and intestinal parasites, is comparatively harmless to man in such quantity as might be taken into the system in the prepared drinking-water. The use of copper would have no influence in retarding the use or establishment of filtration plants, since the copper method is suggested only as an emergency proceeding or supplementary measure, for instance, when the filter is inefficient or there is no filtration system. The experiments of the author were made with weak solutions of copper sulphate, but more especially with colloidal copper. The systematic study of the

organisms which persist, as well as those which are destroyed, is being continued and will be reported upon later. In order to satisfy himself that both colon and typhoid bacilli are destroyed by the presence of copper-foil, the author has made another series of experiments with this particular object in view. From these experiments he draws the following conclusions: 1. The intestinal bacteria, like colon and typhoid, are completely destroyed by placing clear copper-foil in the water containing them. 2. The effects of colloidal copper and copper sulphate in the purification of drinking-water are in a quantitative sense much like filtration, only the organisms are completely destroyed. 3. Pending the introduction of the copper treatment of water on a large scale, the householder may purify his drinking-water by the use of strips of copper-foil about three and a half inches square to each quart of water, this being allowed to stand overnight at an ordinary temperature, and then drawn off or the copper removed.—*American Journal of Pharmacy*, 1904, No. 12, p. 574.

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**The Treatment of Asthma.**—DR. G. AVELLIS divides antiasthmatics into four classes: 1. The preparations of stramonium and the nitrites. 2. The iodides. 3. The preparations of atropine. 4. The preparations of periploine. A fifth class may be made up of the various substances which may be administered by inhalation. The author gives certain indications for the employment of these various classes of remedies. When the attack of asthma is terminated by an abundant secretion of mucus the preparations containing iodides are to be used. When there is little secretion, even when there is cough, the iodides are useless, and the preparations of atropine or belladonna should be used. The cases which may be benefited by the iodides are more common than those in which the belladonna preparations are indicated. All the various asthma powders act in the same way. When one preparation has lost its effect on account of the establishment of tolerance, another will often give relief. Fumigations are particularly effectual in children at the beginning of attacks early in the night. They may then be given without awakening the patient, but their habitual use as a preventive is to be advised against. Asthma, when the attacks are seldom and are separated by intervals entirely free from symptoms, may be favorably affected by the above-mentioned remedies, but when we have an asthma in which the respiration is never free from rales, with constant dyspnoea, no secretion of mucus, and increasing frequency of attacks, we must have recourse to other therapeutic methods.—*Münchener medicinische Wochenschrift*, 1904, No. 43, p. 1923.

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**Fat in Tuberculosis.**—DR. RENE LAUFER considers that the beneficent influence of fats in tuberculosis, as in health, is due to the retention and conservation of nitrogenous substances. He states that when fats are given to tuberculous patients the total elimination of nitrogen is at first lowered and then remains constant. Then fat beyond a certain quantity is not utilized, at least as far as its action upon the conservation of the albuminoids is concerned. Fat, however, to a certain extent, may be deposited in the tissues. The author finds that from 3 to 5 ounces of fat daily (cod-liver oil, butter, olive oil) cause the weight to slowly increase and produce a definite and certain good effect, while larger quantities are followed by a quicker gain in weight, which, how-

ever, is not permanent. Fat more than 3 to 5 ounces daily is, therefore, harmful, and consequently one should ascertain the quantity of fat ingested by the patient before prescribing other fats—cod-liver oil, for instance.—*Revue de thérapeutique*, 1904, No. 22, p. 780.

**The Therapeutic Action of Amyl Nitrite.**—DR. A. VAQUEZ states that a small dose of amyl nitrite given by inhalation to an individual whose arterial tension is moderate results in a diminution of the tension by from 4 cm. to 5 cm. of mercury. A large dose lowers the tension by from 7 cm. to 8 cm. A massive inhalation, on the contrary, habitually causes within fifty seconds a reactionary hypertension, which exceeds the initial tension by from 4 cm. to 5 cm. Consequently, the therapeutic dose of the drug by inhalation should be small—5 to 6 drops. Its administration in capsule is badly borne and produces neither lowering of arterial tension nor diminution in pulse rate. In conclusion, it may be said that in order that the drug may have its proper action it must make a sudden entrance into the organism and take it, so to speak, unawares.—*La presse médicale*, 1904, No. 88, p. 702.

**Thiocol in Tuberculous Conditions.**—DR. SZABOKY considers thiocol one of the best of creosote preparations. In intestinal tuberculosis its use in several cases brought about a normal condition and number of stools in about two weeks. In laryngeal tuberculosis the author has used thiocol internally and locally as an insufflation in combination with boracic acid and cocaine in a few cases, with uniformly good results. In bronchitis and bronchiectasis the expectoration, under the administration of thiocol, became less profuse, the cough less frequent, and the general condition and appetite better, within a few weeks. The author considers the preparation to be an important addition to our armamentarium, since it is pleasant to take—given in orange syrup—does not disturb the digestion, and when given early in pulmonary tuberculosis, before much destruction of tissue has taken place, exercises a favorable influence upon the inflammation, lessening the secretion, cough, fever, and hyperidrosis, and increasing the weight. The dosage is  $7\frac{1}{2}$  grains four times a day.—*Wiener klin. Wochenschrift*, 1904, No. 42, p. 1085.

**Sodium Citrate in the Digestive Disorders of Infancy.**—M. VARIOT reports good results obtained from the use of sodium citrate added to milk in infant feeding when gastric disorders, especially vomiting, are present. The theory is based upon the experiences of WRIGHT, who has shown that if sodium citrate is added to milk the coagulum is less solid and lighter than in the absence of this substance. This action is due to the fact that in the presence of sodium citrate the calcium salts, especially the chloride, which augment coagulation, are precipitated.—*La presse médicale*, 1904, No. 85, p. 679.

**Treatment of Albuminuria by Physical Methods.**—DR. A. STRASSER states that massage in albuminuria ordinarily causes a disappearance of the cedema and increases the quantity of the urine. At first the massage increases the number of casts, but only at the beginning, for the increase in diuresis loosens the casts accumulated in the diseased kidney. Later in the treatment the casts diminish. CASARETTI's method consists in the application of elastic bandages to the lower limbs. Increase

in the quantity of urine results, due to an increase of the intrarenal pressure. In acute nephritis the action of the skin is likely to be defective, consequently hydrotherapeutic procedures are contraindicated; but if uræmic crises are anticipated, hot baths, followed by wrapping in a hot, dry sheet may be given, which will produce profuse diuresis. In the chronic form of the disease baths of hot, dry air, followed by a spray douche, will tone the cardiovascular apparatus. Light, sun, or mud baths may be given, but extremes of temperature are to be avoided. The influence of climate is limited, but life in hot, dry countries may diminish the albuminuria. To sum up, the treatment of albuminuria by physical means is indirect. Its principal result is to increase the power of resistance of the body against the effects of the toxic condition due to a pathological state of the kidneys.—*Blätter für klinische Hydrotherapie*, 1904, No. 10, p. 221.

**The Treatment of Cardiac Patients.**—DR. A. HECHT states that in the treatment of heart cases it is necessary not only to strengthen the heart muscles, but to keep up the patient's nutrition. Consequently the giving of drugs likely to interfere with digestion is to be avoided in so far as possible. Unfortunately these cases are prone to suffer from a poor appetite, which drugging often increases. Digitalis, especially, when introduced into an atonic stomach is likely to remain in the organ a considerable period and to excite nausea; on this account it should be given with agents which counteract this effect. The author recommends the following formula: Powdered digitalis and quinine hydrochlorate, of each 20 grains; extract of nux vomica, 4 to 7 grains. To be divided into 30 pills. One pill 3 times a day. This prescription does not disturb the stomach and the action of the digitalis is augmented by the other drugs.—*Therapeutische Monatshefte*, 1904, No. 8, p. 403.

## OBSTETRICS.

UNDER THE CHARGE OF

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**Moulding of the Fetal Cranium before Birth.**—PLANCHU (*Lyon médical*, 1904, vol. ciii., No. 52) reports the case of a young primipara with rachitic pelvis, delivered by Cæsarean section just before term. The fetal head was lying in the transverse diameter at the brim, greatly overlapping the symphysis and freely movable. The operation was performed before labor pains began. The placenta was behind the anterior uterine wall, but the section presented no other complication.

The infant's head showed marked asymmetry. The left parietal bone, which lay next the symphysis pubis, was flattened and its emi-

nence nearly effaced. The parietal slightly overlapped it at the sagittal suture. The right parietal bone had an increased curvature, its eminence projected, and below this a wide depression ran anteroposteriorly near the temporoparietal suture. The right side of the head was much higher than the left, and the right parietal eminence lay in the plane anterior to the left. When the infant was five days old these deformities disappeared. This moulding is attributed to the pressure of the head against the brim maintained constantly during the last month of pregnancy and largely caused by the muscular contractions of the anterior abdominal wall. It would be difficult, however, to clearly explain this deformity.

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**Tetanus in Pregnancy.**—SCHMIDTLECHNER (*Zentralblatt für Gynäkologie*, 1905, No. 4) reports the case of a woman, aged forty-four years, admitted to the clinic at Budapest in a pregnant condition and suffering from tetanus.

The patient had had eight normal pregnancies and confinements. During the last two she had observed a stiffness in one finger, motion of the hands was impaired, and they seemed as if made of wood. The patient had always been emaciated and not strong.

For five weeks before admission the patient had been very ill, having repeated and painful cramps, loss of appetite, and frequent vomiting. Her strength was so reduced that she moved with difficulty.

On examination she was seven months pregnant, much reduced in weight, and of inferior intelligence. The muscles were badly developed, her complexion was yellowish, the skin pigmented. She had a pulmonary catarrh; her heart was normal. Her temperature was normal; her pulse 132, rhythmical and full. The urine was normal. The position of the fœtus, the size of the uterus, and the child's heart sounds were normal for the period of pregnancy. In the left inguinal region there was a bubo, from which foul pus escaped. In the left gluteal-region there was a bed-sore, and one larger extending to the muscles upon the right side.

The patient was perfectly conscious, and the muscles of the face were not in spasm. The upper extremities were flexed tightly against the thorax and could not be extended. The hands and fingers were flexed, and the patient could not move the fingers. The right foot was extended, the left leg flexed at the knee. When the patient lay upon her back the left knee was in apposition with the right thigh and could not be extended. The patient complained of frequent painful spasm of the upper extremities. On examination the reaction of the galvanic current was greatly increased. Attacks of tetanic contraction of the muscles lasted for about an hour, after which the muscles relaxed and the patient could move the limbs. Under the use of morphine the pain grew less, but the contractions remained the same. Chloral hydrate was equally ineffectual. It was determined first to improve the patient's general condition, to remove the bubo, and to try to heal the bed-sores. Accordingly, the patient was given a generous diet, with alcoholic stimulants, until on the fifth day after admission labor occurred. A male child, 40 cm. long, was expelled living, and two hours afterward the placenta was expressed. Following the emptying of the uterus, the patient's spasmodic attacks ceased, and her pains disappeared. Some of the phenomena of tetanus were increased, and the patient was greatly prostrated.

On the third day after delivery she had an attack lasting three hours, characterized by intense pain, and could retain no nourishment by either the stomach or the bowel. On the following day the patient died cyanotic.

On section the extremities were in a position of marked deformity. The membranes of the brain were anæmic, the cerebral vessels thin and collapsed. The cortex of the cerebrum was atrophied; the ventricles were dilated; and contained clear, yellow serum. The ependyma was smooth and glistening; the substance of the brain was moderately filled with blood, but the brain seemed as a whole dry and somewhat toughened in consistency. The pons and medulla were normal.

The lungs were not retracted, the pericardium was not free, the pleuræ were dry, and the lungs entirely free. Serum was found in the pericardial sac; the heart was not enlarged, its muscles pale brown. The bicuspid valves and the chordæ tendineæ were much thickened and shortened. The lungs were large for the size of the patient, and upon section emitted a thin, seromucous fluid. At the left apex there was an encapsulated mass. The kidneys were pale and atrophic.

The endocardium was covered by a dirty but not diphtheritic secretion. The bladder was pale red, and near the trigonum there was an ulcer.

The results of the autopsy showed a former endocarditis, with insufficiency and stenosis of some of the orifices and brown atrophy of the heart muscle. The ulcer in the bladder was thought to be diphtheritic in character. The spinal cord was not removed.

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**Puerperal Eclampsia Treated by Thyroid Extract Dissolved in Saline and Given Subcutaneously.**—In the *Journal of Obstetrics and Gynecology of the British Empire*, November, 1904, MACNAB reports the case of a primipara, eight months pregnant in eclampsia in her fifth convulsion. The patient was treated by the free use of morphine and external heat, and perspired freely, but continued to have convulsions. Croton oil, calomel, and other purgatives were administered. The convulsions still continued, and sodium bromide and chloral were added. As these measures failed to modify the convulsions, 75 grains of thyroid extract were dissolved in two pints of normal salt solution, and the whole quantity injected beneath each breast. In an hour and a half labor occurred, and under chloroform the child was extracted by forceps, the placenta removed, and the patient allowed to bleed freely. The child was dead. The patient remained in a partially conscious condition for forty-eight hours and then developed pneumonia at the right base, from which she recovered. So far as could be ascertained, the patient had thirty-seven convulsions.

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**A Simple Method for Performing Embryotomy.**—SEELIGMANN (*Zentralblatt für Gynäkologie*, 1905, No. 3) calls attention to the difficulty which a physician without competent assistance and without an operating table may experience in performing embryotomy. This is especially true in shoulder presentations, with prolapse of the arm, where decapitation must be performed. He found the following procedure useful in these cases:

The patient having been placed across a bed and the bed made as high as possible, the operator prepares his instruments, which consist



of a long-handled strong pair of blunt-pointed scissors and the usual decapitation hook or sling. The operator then pulls firmly upon the prolapsed arm until the thorax has been drawn down as far as possible into the vagina. He then opens the chest of the foetus at the point which is lowest, making a free opening. He then eviscerates the thorax as thoroughly as possible and gives a copious douche of 2 per cent. lysol; introducing the fingers of the left hand into the thorax, he carries the fingers through the muscles upon the posterior aspect of the chest, and, introducing the hook with the right hand, guides it with the fingers of the left until the hook is carried around the vertebral column of the foetus. By strong traction the vertebral column is then severed and the hook is removed. The fetal body collapses, and the tension upon the lower uterine segment is at once relieved. In some cases the fetal head, unless strongly attached to the child, is gradually expelled by the effort of the mother. In other cases version is performed, followed by extraction.

He reports two cases illustrating this method. The first was that of a multipara with normal pelvis, who had a shoulder presentation, with prolapse of the left arm and pulseless umbilical cord. The uterus was firmly contracted. It was impossible to dislodge the foetus without great danger of uterine rupture. Under anaesthesia, embryotomy was practised by the method described, the breech of the child was brought down and the head brought through the pelvis by suprapubic pressure. The mother made a good recovery.

A second case was that of a primipara with flat rachitic pelvis, the true conjugate being 8.5 cm. The foetus was in transverse position, the back to the right, the left arm prolapsed, and the umbilical cord pulseless and prolapsed. The lower uterine segment was greatly distended. After the spinal column had been severed the left arm was amputated at the shoulder and the remainder of the foetus delivered by version and extraction. The mother recovered.

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**Cæsarean Section.**—OLSHAUSEN (*Zentralblatt für Gynäkologie*, 1905, No. 4) reports two Cæsarean sections, one for symmetrically contracted pelvis, the other in a primipara after nine severe eclamptic convulsions. Both patients recovered. Olshausen has performed between 80 and 90 Cæsarean operations, of which 7 have been done for eclampsia; 6 of these recovered, 1 died. He has used catgut only for suture in these operations.

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**Repeated Cæsarean Section, with Fatal Result.**—TREUB (*Zentralblatt für Gynäkologie*, 1905, No. 3) reports the case of a patient with a highly contracted rachitic pelvis, who was delivered by Cæsarean section in her first pregnancy ten years previously. From this she made a good recovery.

The second section was performed five years later, and recovery followed, with slight rise of temperature. In the third pregnancy the patient was admitted to the hospital for operation, and no vaginal examination was made. The temperature before operation was between 99° and 100°. Upon section wide adhesions were found between the colon and the uterus. The operation proceeded smoothly, and because of the adhesions both Fallopian tubes were resected to

prevent further pregnancy. Death from acute peritonitis followed a few days later.

At autopsy the wound in the uterus was smooth and well healed. Infection had arisen from some source outside the uterus, probably from the intestine, although microscopic examination of the tubes showed the characteristic appearances of acute inflammation, with abundant proliferation of leukocytes. At the second section the abdomen was perfectly normal.

This case draws attention to the propriety in highly contracted pelves of rendering further impregnation impossible at the first Cæsarean section.

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## GYNECOLOGY.

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UNDER THE CHARGE OF

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ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

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**Torsion of Parovarian Cysts.**—**VAUVERTS** (*Annales de gynécologie et d'obstétrique*, February, 1905) has collected reports of 20 cases, 1 of which occurred under his own observation. The rarity of the accident is due to the fact that these cysts seldom have long pedicles. It is as common on the left as on the right side. The youngest patient was fourteen years of age, the oldest fifty-two. In 2 cases torsion of the pedicle occurred during pregnancy, in 1 after premature delivery.

The results of the torsion were varied. Usually hemorrhage took place into the cyst, and its wall was often gangrenous, the seriousness of the condition varying with the degree of torsion. As Binelly has observed, the comparative absence of pathological changes has been due to the thickness of the pedicle and the fact that the circulation was not entirely interrupted. The ovary seldom participates in the torsion, and is usually merely congested; the same applies to the tubes. In some instances localized peritonitis was noted. In 1 there was obstruction of the gut by the cyst.

The clinical symptoms were sudden acute pain and later peritonitis, with vomiting, fever, rapid pulse, and tympanites. The symptoms may subside in a few days and entirely disappear. If adhesions form, the cyst becomes fixed, and may increase in size.

Recurrence of the symptoms may take place, due either to untwisting (*détorsion*) of the pedicle or a new torsion. The only treatment is laparotomy, pregnancy not being a counterindication.

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**Absence of the Vagina.**—**VAUTRIN** (*Annales de gynécologie et d'obstétrique*, February, 1905) concludes an article on this subject with the statement that complete absence of the vagina is a curable mal-

formation and is not an absolute ban to marriage. Hæmatometra and hæmatosalpinx may be prevented by operation. The best operation is incision and autoplasty with their juxtaposed flaps. Snéguireff's plan of utilizing part of the rectum is too complicated and has serious inconveniences.

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**Vaginitis in Children.**—LUTAUD (*Revue prat. d'obstétrique et de gynécologie*, February 14, 1905) calls attention to the fact that little girls may contract blennorrhœa, not only by sleeping with older persons, but from the seats of water-closets, steps, etc., because their genitals are not properly protected. It is not necessary to infer that they have become infected by sexual intercourse, since there are many opportunities for impure contact with the linen of nurses who have gonorrhœa. The prophylaxis consists in careful washing of the hands before bathing the genitals of children and insisting that they do not wear open drawers.

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**Etiology and Transmission of Cancer.**—LUTAUD (*Revue prat. d'obstétrique et de gynécologie*, February 14, 1905) concludes that cancer is a constitutional disease, and that it is neither inoculable nor contagious. It always has a local origin due to abnormal cell proliferation, which at the onset does not differ from the proliferation of benign tumors.

The gravity of the prognosis is due to the fact that the tumor is not encapsulated and the accompanying lymphatic involvement. Leukæmia seems to favor the rapid development and generalization of cancer.

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**Sterilization of Cutting Instruments.**—ROYSTER (*Annales of Gynecology and Pediatrics*, February, 1905) concludes a series of experiments and inquiries addressed to different operations, with the following inferences: 1. Knives can be thoroughly sterilized without the use of heat. 2. Most American surgeons use carbolic acid or alcohol, or both. 3. Boiling is most apt to render the edge of the knife dull, 95 per cent. alcohol least so.

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**Syphilis of the Adnexa.**—PICHEVIN (*Gazette des hôpitaux*, 1905, Nos. 1 and 2) says that syphilitic disease of the tubes and ovaries is now so rare as to be considered by many observers as problematical. He bases his diagnosis largely on the diminution of enlarged and tender ovaries under specific treatment. Not only have true gummata been found in these organs, he affirms, but the sclerosis anatomically characteristic of syphilis. Only 3 undoubted cases of syphilitic salpingitis had been described until Watthieff published 5 others. All were characterized clinically by intense local pain, especially at night, associated with menorrhagia. The usual anatomical changes were gummatous or purulent.

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**Postoperative Gastric Paralysis.**—REYNER (*Revue prat. d'obstétrique et de gynécologie*, 1904, No. 11) calls attention to the fact that many of the symptoms of this condition are small and frequent pulse, tympanites, and an anxious expression. However, patients with simple gastric paralysis have only hicough, without vomiting, though they may occasionally raise a black fluid which may be mistaken for fecal. The more fluids are given, the greater becomes the distention.

[The writer reports several cases in which the use of the stomach tube speedily relieved symptoms that appeared to be of the gravest character. He urges that it be introduced as soon as the symptoms appear.]

There can be no doubt as to the value of gastric lavage after abdominal section. In this country it is the habit with many surgeons to wash out the stomach before the patient leaves the operating table, and in any case if distention or obstinate hiccough, regurgitation or vomiting persist during the first forty-eight hours. It must not be forgotten that true acute dilatation of the stomach has been described as a cause of death after laparotomy, though, as in a recent case in our practice, it is probable that there is no permanent anatomical change in the capacity of the stomach.—H. C. C.]

**Primary Cancer of the Fallopian Tube.**—TOMSEN (*Journal d'obstétrique et de gynécologie de St. Petersburg*, 1904, No. 11) adds another case to the 54 previously reported. The patient, aged twenty-nine years, had been operated upon eight years before for hydrosalpinx (stomatoplasty), and returned complaining of metrorrhagia and a purulent discharge from the vagina, with severe pains in the lower abdomen. A hernia existed at the lower angle of the abdominal cicatrix, in which was a painful induration. On operation the latter was found to be a left tube fixed to the abdominal wall and bladder. The right adnexa, being normal, were not disturbed. Examination of the specimen showed atypical cell proliferation. Two months later recurrence had occurred in the pelvis and abdomen, so that an explorative incision alone was possible.

**Lymphangioma of the Peritoneum.**—HELLIER (*British Medical Journal*, November 12, 1904) reports the case of a multipara, aged thirty-four years, with an elastic abdominal tumor, independent of the uterus, which was supposed to be an ovarian cyst. On opening the abdomen, a conglomeration of cysts was found in the omentum, bearing no relation to the pelvic organs. Similar cysts were present in the parietal peritoneum. The patient made a good recovery, and was well four years later.

The neoplasm was supposed to be malignant, but on microscopic examination found to be composed of myxomatous tissue containing large cavities.

**Paralysis of the Non-pregnant Uterus.**—KOSSMANN (*Zentralblatt für Gynäkologie*, 1905, No. 8) concludes a paper on the subject with the inference that many of the cases of perforation of the non-puerperal uterus with the sound or curette in the hands of skilful operators must be explained by paralysis of the muscle. Further observations are necessary in order to determine the exact state of contractility of the muscle at the time of the accident.

**Adrenalin in the Menorrhagia of Puberty.**—TREDGOLD (*British Gynecological Journal*, 1904, No. 11) cites the case of a girl, aged thirteen years, whose first menstruation lasted five days. Later she flowed so excessively as to become exsanguinated. The pelvic examination was negative. Opium and ergot were administered without benefit. The

writer finally tried 15-drop doses of 1:1000 adrenalin, with 10 drops of cannabis indica, every two hours. After the second dose the pulse dropped, temperature diminished, and at the end of twelve hours the hemorrhage ceased. After forty-eight hours the treatment was discontinued, and rapid convalescence ensued. The periods were subsequently entirely normal.

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**Consent of the Patient to Operation.**—The question raised by CHROBAK is further discussed by DUBROSEN in the *Zentralblatt für Gynäkologie*, 1905, No. 8. His own unpleasant experience with damage suits and that of his colleague have led him to require each patient previous to operation to sign a paper giving him full authority to complete the operation according to his best judgment.

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**Remains of the Wolff-Gartner Duct.**—LEISEWITZ (*Zeitschrift für Geb. und Gyn.*, Band liii., Heft 2) reports an interesting case in which ulcerated nodules developed in the vaginal fornix of a multipara, aged forty-two years. As malignant disease was suspected, one of the nodules was excised and examined microscopically, with negative results. The uterus was then extirpated, on the ground that the tumor might be cancerous degeneration of the paravaginal remains of Gärtner's duct.

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**Colpotomy for Puerperal Peritonitis.**—GUÉNIOT (*Transactions Société d'Obstétrique de Paris*, 1904) thinks that since abdominal section for the relief of this condition is almost certainly fatal, vaginal incision (without anæsthesia) offers an equally good means of drainage with less risk to the patient. In the discussion of this paper Jeannin took the ground that the abdominal route was not much more dangerous than the vaginal and permitted direct inspection and more thorough toilet of the peritoneal cavity.

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**Aspirin in Obstetrics and Gynecology.**—GOTH (*Gyegyszazat; Zentralblatt für Gynäkologie*, 1904, No. 38) was led to try this drug from his observations of its analgesic action in rheumatism. In labor it relieves pain without diminishing uterine contraction. In 276 gynecological cases the writer obtained the best results in inoperable carcinoma, dysmenorrhœa and disease of adnexa, also as a means of relief in painful uterine contraction after operation. He gives 7 grains every half-hour up to four doses; 15 grains are given at a dose in cancer cases. Unpleasant symptoms were observed if upward of 45 grains were given.

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**Degeneration of the Graafian Follicles.**—BOESLIAGEN (*Zeitschrift für Geb. u. Gyn.*, Band liii., Heft 2) summarizes the results of his examination of 50 ovaries as follows: The variations in the degenerative changes in the follicles are due both to the ingrowth of the surrounding stroma and the hyaline changes in the same. The cells of the theca interna are quite similar to the so-called lutein cells. According to the predominance of either change there may result a corpus fibrosum, or corpus albicans, or a simple corpus atreticum may be formed. Through the degeneration of large corpora lutea a hypertrophied corpus fibrosum or corpus albicans may occur. Cells derived from the theca

persist for a long time, and as these resemble lutein cells so closely, these may apparently exist in the midst of perfectly normal stroma. Hyaline degeneration of the theca in the normal ovary is closely related to similar degeneration of the surrounding arterioles, so that the latter cannot be regarded as strictly a pathological process.

**Constipation as a Cause of Intrauterine Infection.**—CAPALDI (*Arch. di ost. e gin.*; *Zentralblatt für Gynäkologie*, 1905, No. 8) conducted a series of experiments in animals in order to determine the effect of coprostasis on uterine infection. Complete obstruction was produced by suturing the anus. Both pregnant and non-pregnant guinea-pigs were used. Almost without exception colon bacilli were found in the uterus, amniotic fluid and peritoneal cavity after death. Although these experiments do not furnish conclusive evidence with regard to the effects of obstinate constipation in the human female, the writer believes that they point a moral as to the importance of careful regulation of the bowels in the non-gravid as well as in pregnant women.

[Another evidence of the importance of the question of intestinal toxæmia which gynecologists and obstetricians are beginning to appreciate.—H. C. C.]

## OPHTHALMOLOGY.

UNDER THE CHARGE OF

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**Some Considerations upon Primary Keratoconus.**—WICKERKIEWICZ (*Arch. d'oph.*, February, 1905) discusses certain doubtful points in the pathology and course of this affection.

The form consecutive to other diseases is not very rare; it is less easy of explanation than the primary. The latter is of rare occurrence. Both eyes are usually, though not always, affected.

It is uncertain when primary keratoconus was first described; even to this day the two forms are confounded. A Tübingen dissertation of the year 1748 by Mauchart, under the title of "Staphyloma Diaphanum," appears to show the first traces of a certain diagnosis. It seems beyond doubt that keratoconus is not necessarily congenital, as Ammon believed, but its mode of origin has not been satisfactorily explained yet. It has been generally attributed with Arlt to a diminution in the resistance of the cornea. Opinions differ as to the causes of this supposed weakening. By some this weakening is ascribed to the corneal tissue, by others to defective innervation, while still others invoke increase of tension; but even if any or all of these conditions are present, no one has shown how they have come to pass. As a matter of fact, careful examination does show

a very slight increase in the tension; but the latter is in itself inadequate, without the presence of another factor, to cause the cornea to yield. What is this factor? This point has not yet been adequately cleared up. It is not inflammation (Stellwag), nor a lesion of the endothelium (Panas). Wickerkiewicz believes that it is a disturbance in the nutrition of the tissues which affects the central portion of the cornea, generally the thinnest part of that membrane. Traumatism has also been invoked as the original cause of keratoconus, but this has not been proven.

It is generally stated that the centre of the cornea becomes conical. But it is not the very centre itself which yields, but a neighboring region, situated, as a rule, at the inferoexternal portion of the cornea. How explain this fact? Gullstrand invokes the excess of extraocular pressure over the intraocular tension. Wickerkiewicz considers such inequality to be due to the pressure of the upper lid upon the globe; this becomes all the greater because of the myopia which results from the development of the cone and the patient's consequent attempts to cut off the disturbing peripheral rays by the lids. Such pressure favors the displacement downward of the apex of the cone.

Based upon experiments upon rabbits, it is held by some that the cone develops in consequence of an ectasia after a wound of the endothelium and basal membrane, while others regard it as due to an œdematous thickening of the cornea. It is difficult to apply these conclusions to the human eye, the cornea of which is thinnest at the centre, where its resistance is feeblest.

Of a special and rare phenomenon which has been occasionally noted, viz., rhythmic variation in the size of the images due to a pulsation of the apex of the cone, Wickerkiewicz was at first inclined to explain the phenomenon by slight movements of the head caused by the beating of the pulse; in one case, however, the ophthalmometer showed objectively continual rhythmic variations in the reflected images, due to rhythmic changes of form in the apex of the cone. This pulsation is analogous to what occurs where an opening leads to a cavity surrounded by fixed walls and containing vascular tissues or liquids. This is precisely the case in an eye affected with keratoconus. The opening is represented by the anterior chamber's extension into the cone; the cavity surrounded by fixed walls is the interior of the eye with its choroidal and retinal lining. That this phenomenon is not present in every case is due to the fact that the ectatic cornea is not sufficiently thinned to permit its appearance.

The diagnosis of keratoconus, even in its first beginning, is easy by means of skiascopy.

The writer has obtained good results from iridectomy in some cases, and the galvanocautery in others. The number of his personal observations is too few to permit him to pronounce definitely upon the respective values of caustics, the cautery, and iridectomy.

**The Neuritic Form of Albuminuria Retinitis.**—BALLENTINE, Glasgow (*The Ophthalmoscope*, April, 1905), calls attention to the rarity of optic neuritis as the only ophthalmoscopic change in Bright's disease. The typical ophthalmoscopic picture is one of prominent inflammation of the optic disk not extending into the surrounding retina; in fact, closely resembling choked disk of intracranial tumor, for which it

has been mistaken. These cases, in fact, emphasize the importance, if such were needed, of a thorough examination of the urine before making a diagnosis of cerebral tumor. The oedema of the nerve may have its origin in a rise of intracranial pressure, due, perhaps, to excess of fluid in the lateral ventricles of the brain. Gowers believes that such cases show slight retinal changes—hemorrhages, spots of exudation—sufficient to distinguish them from those of cerebral neuritis. These slight changes are easily overlooked. Cases presenting this ophthalmoscopic picture have usually shown mental or cerebral symptoms suggestive of intracranial tumor. Gowers states that the class of cases in which the neuritic form of albuminuric retinitis occurs are cases of advanced chronic kidney disease, usually of contracted kidney. It is a grave prognostic, soon followed by a fatal result.

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## OTOLOGY.

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UNDER THE CHARGE OF

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**Influence of the Cure of Suppurative Otitis Media on Concomitant Mental Affections.**—J. TOUBERT (*Ann. des mal. de l'oreille*, etc., 1904, T. xxx., No. 5) states the fact that the influence of nasal affections in general on the nervous system have long been known, and that, beginning with the self-observation of Ziem, which dates back to 1884, systematic investigation has been made into the influence of suppuration of the neighboring cavities of the nasal fossæ, upon the mental state of the patients, led him to take up comparative studies of the same nature made in otology and to make researches into the influence of diseases of the ear on the nervous system in general and on the mental state of the patient in particular.

In pursuit of this purpose the author perused the classic works and periodic publications devoted to otology, neurology, and to psychiatry, and, while finding anthropologic studies on the shape of the auricle in the insane and in degenerates, studies on the frequency and the pathogeny of othæmatoma in the same class of patients, researches on hallucinations due to the auditory apparatus, detailed descriptions of disorders of sensibility, of hysteric or epileptiform manifestations in which the cause was a superficial or a deep lesion, a dry or suppurative disease of the ear, and, finally, sensory, motor and even psychic disorders, referred to intracranial complications of suppurative otitis, discovered, in the domain where otology borders on psychiatry, but little of particular importance since the time of the eminent work of Albert Robin of twenty years ago.



In view of this lack in otological literature, the author reports two cases, coming under his personal observation, terminating in simultaneous cure of the chronic suppurative otitis and of the insanity, and adds analogous clinical facts found in various publications, grouping them and drawing conclusions from their comparative study.

A common clinical picture is that of a patient afflicted with an otitis to which he does not, at first, pay much attention, presenting later psychic disorders of such character that he is considered deluded or insane and sometimes confined as such, the otitis and the insanity continuing to evolve. Finally, at the end of a variable time (1) either the insanity is cured in spite of the otitis persisting; (2) or the insanity persisting, the otitis is cured spontaneously or through remedial intervention; (3) or the insanity disappears coincidently with the cure of the otitis.

All of the observations made personally by the author, or collected from medical literature, come under one or the other of these three categories. Cases where, properly speaking, there was no question of mental disorder, as, for example, those post-otitic symptoms of neurasthenia well known in otology, and which Gellé especially has reported as frequently observable at the Salpêtrière after epidemics of la grippe are excluded; but, on the other hand, cases where the momentary cessation of the otitis has actually aggravated the mental state have been included.

*First Group of Observations: Psychic Cure without Otitic Cure.* In this group there were found in the literature without doubt in consideration of pathogenic interpretations of which they might be the object, only the cases where the persistence and even the return of the otitis coincided with the disappearance of the mental phenomena. No doubt there are cases, more numerous yet, where these phenomena improved without change in the progress of the otitis.

1. (Case of Linden.) Related by Urbantschitsch, in substance: A patient was afflicted with mania, at the same time that an otorrhœa stopped. The maniacal disturbances disappeared, eight days later, coincidently with re-establishment of the purulent discharge; the memory returned likewise.

2. (Case of Urbantschitsch.) A patient treated for chronic suppurative otitis. A young man, modest and quiet, had at first painful sensations and some pain in the ear and then manifested excitability which reached insanity. A day or two later, a more abundant discharge from the ear appeared and his usual psychic state returned.

3. (Case of Doutribente.) Related briefly by Alb. Robin. A traveling salesman, aged forty-two years, who had twice been an inmate of the asylum at Blois and who had been suffering from an otorrhœa for ten years. In this case delirium appeared as soon as the discharge stopped and recovery had twice coincided with the return of the purulent discharge from the ear.

4 and 5. (Cases of Schüle and of Fuerstner.) Fuerstner relates a case of Schüle's where a psychosis retroceded immediately upon the appearance of a profuse purulent otorrhœa, without prodromal symptoms. Fuerstner observed a similar case.

*Second Group: Absence of Psychic Recovery and Otitic Recovery.* Under this heading there is an absolute lack of published reports of cases. It is, however, without doubt, among the ever-increasing

population of the lunatic asylums, that the spontaneous cure of otitis is not absolutely exceptional. On the other hand, since it is recognized that the insane are entitled to the benefits of general or special surgery in an equal degree with other patients, otorrhœas which justify surgical intervention are operated upon, and the majority of these otitic affections are remedied by the petromastoid exenteration. In the asylum of the Seine alone more than 20 cases of this kind have been successfully operated upon and, as these cases have remained unpublished, it is probable that the same is true of a number in other institutions which have disappeared in forgetfulness, through lack of published reports.

*Third Group: Psychic Cure and Otitic Cure at the Same Time.* This group is most rich in reported cases, not (unfortunately for the rest) because these cases are the most frequent, but without doubt because they are more interesting, more satisfying, more flattering to the doctor or surgeon, and have solicited, spontaneously, the honor of publication.

In certain of the cases the mental symptoms, although violent, were of a temporary nature and the cure appears but little merited; in others, the insanity had required incarceration of a duration terminating with the cure of the otitis—that is to say, sometimes a long period of time. In some of the cases absolute cure was questionable, although there was considerable improvement.

1. (Case of Bouchut.) A boy, aged six years, was attacked by “a heavy catarrh of the right ear, which had been suppressed by the last exposure to cold.” There were intermittent attacks, without fever, with sudden access of delirium “presenting the characteristics of insanity;” there was “complete loss of memory, acute delirium, accompanied by striking, abusing his parents, whom he did not recognize, crying, beating the furniture in the room, talking to the wall, which he took to be alive.” Morphine was given, vesicants were applied over the mastoid process and emollient injections were made into the auditory canal. Three days after this treatment the patient became calm, there was re-establishment of the discharge, which finally ceased, and the case was discharged cured.

2. (Case of Bouchut.) A boy, aged ten years, sick for three months; great pain in the right ear accompanied by a purulent discharge. Attacks at first few, then frequently and of frightful violence; excitement, cries, howling like a dog; tendency to bite people who approached him and to destroy all objects which came in his way. Bromides, chloral, chloroform, and sulphate of quinine were given and the attacks lessened in frequency and severity and the discharge from the ear ceased.

3. (Case of Ménière.) A child, aged five years, with a mucopurulent discharge from the right ear of three years' duration, with destruction of the drumhead and ossicles, with exception of the stapes. The attacks of delirium occurred without apparent cause, accompanied by violent anger and a tendency to beat everything within reach. The treatment consisted in the local application of carbolized glycerin, with resultant slight local improvement and diminution of the attacks, at which stage the case passed from observation.

4. (Case of Rhyss Williams.) A man, aged thirty-six years, with a purulent discharge from the left ear of several months' duration, discovered eight days after entering the hospital. Agitation day and

night, incoherence of speech, hallucinations of sight, for a month before entrance. Then disease of the mastoid for a month, when the patient became so violent and so irascible that it was impossible to examine him. Upon the opening of the mastoid abscess reason returned immediately. The discharge from the ear disappeared completely and cure followed without deafness.

5. (Case of Brown-Séguard and Elmyra.) Cited by Alb. Robin. This patient was believed to have a general paralysis. "M. Brown-Séguard percussed the skull and found the bone very painful about the middle of the mastoid process. This fact recalled the existence of a purulent discharge, and the opening of the mastoid led to complete disappearance of this (pseudo) general paralysis."

6. (Case of Catlett.) A young girl, aged twenty-four years, had acute mania of thirty days' duration with prostration, rapid wasting away, delirium day and night, hallucination of sight (fire) and of hearing (cries of the shipwrecked). These auditory hallucinations "seemed to be the result of the increase of the otitis . . . the mental disturbances and the hallucinations stopped with the subsidence of the otitis. . . ."

7. (Case of Ball.) A young man, aged twenty-two years, with chronic otitis media in the left ear following a blow nine years previously. At the age of sixteen years he had typhoid "with cerebral disturbances, delirium day and night, and marked increase since the discharge from the ear." From time to time he was subject to storms of violence and to impulses accompanying hallucinations of hearing which necessitated his commitment. M. Miot discovered an otitis media with suppuration of the middle ear, perforation of the drumhead, and granulations covering the tympanic mucous membrane. Treatment of the otitis (injections, washes, cauterization) resulted in diminution of the hallucinations and their final disappearance coincidently with cure of the otorrhœa.

8. (Case of Régis.) A man, aged twenty-seven years, had otorrhœa in the right ear, of fifteen years' duration, following a direct trauma; he had been hypochondriacal from infancy, and was haunted by his otitis and by hallucinations of hearing on the diseased side. There was an otitis media, with perforation of the superior part of the drumhead (Miot). Local treatment of the ear was instituted and cautery applied over the mastoid. "Three weeks later the discharge had diminished and the hallucinations were no longer perceived during the day. . . . At the end of a month there was complete cure of the otorrhœa as well as of the hallucinations." After three months, in which time no treatment took place, "the patient was pronounced radically cured of his otorrhœa and of his hallucinations."

9. (Case of Th. Browne.) Cited by Alb. Robin. This patient "had presented signs of insanity when by chance an old otitis was discovered, the cure of which was followed by the disappearance of the mental state which had been of long duration."

10. (Case of J. Toubert.) R. (Marie), under treatment at Villejuif (service of M. Toulouse). The certificate of confinement, signed November 26, 1902, by M. Magnan, read "mental degeneration, multiple hallucinations, alternating excitation and depression;" and a more detailed note, furnished by M. Toulouse, said that "when R. came to the asylum she presented some phenomena of confusion of

ideas, accompanied by very marked agitation and excitement; she had terrifying hallucinations, she screamed, and her state made it necessary to place her in the section for those greatly agitated." The past history of the ear was unknown. On December 6th she was sent to the surgical pavilion, in the service of M. Picqué, for an acute suppuration of the left parotid region, reaching to the upper eyelid, which was incised on the following day. The patient was very anxious, uttered groans, and did not respond to questions; subsequently suppuration of the auditory canal was found and M. Picqué curetted the attic on January 10, 1903. Three distal abscesses of the nature of metastatic abscesses developed: one, very large, on the anterior thoracic wall; two others, smaller, in the deltoid region; these were opened on January 22d.

On February 3d, at the request of M. Picqué, the author examined the patient and found the primary fistula, slightly suppurating, the length of the posterior border of the maxillary bone, and a second corresponding to the superior part of the auriculomastoid furrow. There was marked œdema in the superior carotid region. Suppuration was abundant from the retroauricular fistula and from the auditory canal, and the mental state was negative.

Operation under chloroform. Classic incision in the furrow, periosteum retracted. Cortex explored minutely and found intact. Trepanned at point of election; in four blows on the chisel the antrum was reached and found to be filled with granulomata from which there was profuse hemorrhage, which ceased when the parts were completely curetted. Examination of the central cavity showed the walls to be everywhere solid, and the cavity extensive, especially below.

Following the operation there was rapid diminution of the suppuration, little by little the sinuses closed, and on March 3d the patient left the hospital. At the end of June, 1903, the ear was completely healed.

From the time of operation the mental disturbances changed in character, then slowly passed away, and in a note dated March 26th, addressed to M. Picqué, M. Toulouse, who had taken the patient in his service, described the different phases of the improvement as follows: "March 3d, R. came back to the surgical pavilion in a melancholic state with depression. There were no delirious ideas, but these were replaced, on the whole, by sadness. The patient answered to hardly any questions; she had a bending posture. One week later, at the morning visit, R. spoke and answered questions like a normal person; she smiled and did not seem sad. The nurse of the ward reported that the beginning of the recovery of her mental state had seemed to come on quickly the night before. There was a complete change in her mental state in the succeeding days. . . . Since then the mental improvement has been maintained. R. seems to have come back to her normal state."

11. (Case of J. Toubert, unpublished.) C. (Henry), aged twenty-eight years, confined at Villejuif in the service of M. Marie, with the following admitting diagnosis, written by M. Magnan, November 14, 1902: "Mental degeneration with hallucinations, disturbances of general sensibility, ideas of persecution; fears of poisoning, and threatens his wife." Removed to the surgical wing, in the service of M. Picqué, for right chronic purulent otitis, on November 22, 1902. Two operations were done by M. Picqué. In November, petromastoid exenteration; sclerosis of the wall of the antrum, so that one could not

open it up wholly; the middle ear, filled with granulations, was curetted. On January 18th a secondary operation upon the posterior sinus was done, with free curetting and large posterior drainage.

On February 3d the author saw the patient and operated, with the assistance of MM. Picqué and Dagonet. Classic incision. Detachment of the auricle and canal, piercing of the aditus by Stacke's protector, introduced into the middle ear; enlargement of the mastoid cavity; opening of a large cell; abrasion with the gouge and mallet of the superior half of the upper border of the osseous canal. Some facial twitchings during the operation, but no immediate paralysis—that is to say, when he awoke. The next day paresis; the following day complete facial paralysis, which later diminished; when he left the ward, on March 25th, movements had reappeared in the muscles of the lip and of the cheek; the orbicularis of the eyelid remained paralyzed, the eye half opened, and the folds of the forehead effaced.

Two months later, M. Picqué saw the patient again at Villejuif, cured of his paralysis.

As to his mental state, he progressively and regularly improved. By way of experiment, the patient had been placed at first, for three months, on provisional freedom; then confinement to end definitely in November, 1903. Besides, as a testimonial, a certificate of dismissal from Dr. Marie, couched in the following terms: "Marked mental debility; vague ideas of persecution, with intermittent exacerbations. This improved patient has profited with permission of a trial of three months without accident; a surgical intervention having happily modified his hallucinatory state, he has permission to leave." At the beginning of 1904, M. Picqué received a note of thanks from this patient, who continued to remain well from a mental point of view.

Setting aside the question of mere coincidence, in view of the observed relationship between the psychic phenomena and the suppurative disease of the ear and the coincident relief in the great majority of the cases, there remain a minority of cases to be explained upon the basis of certain hypotheses.

1. *Mechanical Pressure.* The cases included in the first group, where retention of pus in the ear has aggravated the mental state, justify this interpretation, the condition being that in a case reported by Biehl, where hallucinations appeared at the same time that an extradural abscess developed and disappeared after its opening and where the cure was complete. But in the cases elsewhere cited there is nothing indicating the probability of intracranial pressure.

2. Some writers have advanced the hypothesis of anatomical lesions of the meninges, discrete lesions, also curable, with chronic meningitis, dry or serous, for example. Schiffers does not seem hostile to this hypothesis, and Mignon would accept it in certain cases analogous to those which he has reported, very briefly, however, for want of documentary evidence, in his important monograph on the complications of otitis. But up to the present time we rarely make a prognosis of curable meningitis, and in the future it is to lumbar puncture and to bacteriological investigation that we must look to clear up the diagnosis in these cases where this hypothesis could be expressed with probability. At any rate these cases only constitute the exceptions, and among the cases above cited there are few for which this is a justifiable explanation.

3. It seems more prudent to hold to the dynamogenetic action exercised through the medium of the nervous system or of the circulatory system, a suppurative otitis establishing, for the brain, especially in patients predisposed, a permanent cause of irritation, by reflex paths. Moreover, this same inflammatory area could cause circulatory disturbances in its neighborhood or discharge into the circulation toxic products affecting the nervous system. This is why this third hypothesis, which is in part analogous to that admitted by a number of alienists for hallucinations (psychosensorial theory), may perhaps be accepted, at least provisionally, until a better one replaces it.

The conclusion to be drawn, in the opinion of the author, from the perusal of the observations here collected and from facts that have been individually established, is that, in a proportion of cases, in regard to the number of which it is impossible to be precise, but which certainly is too large to be neglected, the cure of otitis in certain of the insane is followed by the cure of mental disturbances. Chronic suppurative otitis being of itself a disease capable of putting life in danger, there is no reason for not attempting to help a patient with an otorrhœa, although insane, by petromastoid exenteration, if that is indicated. To effect a simple cure would be a happy result; to effect a double cure would be an ideal result, and is by no means an impossibility.

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## PATHOLOGY AND BACTERIOLOGY.

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**The Effect of the Bile upon the Ester-splitting Action of Pancreatic Juice.**—HEWLETT (*Johns Hopkins Hospital Bulletin*, 1905, vol. xvi. p. 20), in a preliminary report, gives the results of some experiments which go to show that bile has an accelerating influence upon the ester-splitting action of pancreatic juice. By injections of scerctin pancreatic juice was obtained from dogs. The quantity of acid formed in twenty-four hours by the action of this juice alone upon ethyl butyrate was very small, but if bile were added the cleavage proceeded with greater rapidity, and much more acid was formed. If instead of ethyl butyrate a soluble triglyceride were employed, such as triacetin, additions of bile to the pancreatic juice exerted the same accelerating action as was noticed with ethyl butyrate. The addition of bile also accelerates the action of pancreatic juice upon emulsion of olive oil, but to what extent has not yet been definitely determined. Further experiments went to show that of the various constituents of bile lecithin was the most important, and, perhaps, only substance, which possessed this accelerating

action upon the pancreatic juice. Various suggestions may be offered to explain the method of action between the bile and pancreatic juice. The author inclines to the belief, however, that bile, increases the ester-splitting action of the pancreatic juice by virtue of a zymoexcitor which it contains; and this zymoexcitor is, at least in part, lecithin.

**Adrenal Rests in the Liver.**—The localization of adrenal rests in the parenchyma of the kidney, along the spermatic veins, and in the neighborhood of the main genital apparatus has been recognized, and, indeed, emphasized for some time; but apparently little attention has been called to the presence of these structures in the liver. In an examination of 510 livers Schmorl found adrenal tissue four times, and in a fifth instance discovered an adenomatous tumor the origin of which he attributed to an adrenal rest. Obendorfer has published a description of one similar tumor in the liver, while a doubtful case has been reported by Pepère. Beer (*Zeit. f. Heilkunde*, 1904, Bd. xxv. p. 381) has made a careful examination of 150 livers to determine the frequency of possible adrenal rests in this organ. In 6 of the 150 cases definite areas of adrenal tissue were found. The single masses were about the size of a pea. Usually the appearance was so typical that a diagnosis could be made macroscopically. They were all situated in the right lobe of the liver near the position of the adrenal gland, and all except one were placed in the capsule of Glisson. One rest was found in the parenchyma of the liver.

In this connection de Vecchi (*Virch. Arch.*, 1904, Bd. clxxvii. p. 133) describes in detail a tumor about the size of a nut discovered in the liver of a man dead of pyæmia following brain abscess. The mass lay in the right lobe of the liver at the suprarenal impression, and was bright yellow in color. After careful microscopic study the author concludes that the tumor arose from an adrenal rest composed of cortical cells.

Though several theories are advanced to account for the method by which these portions of adrenal substance become incorporated in the liver, an exact explanation is still wanting.

**The Protozoon of Scarlet Fever.**—DUVAL (*University of Penna. Med. Bulletin*, 1904, vol. xvii. p. 298) makes a preliminary report upon certain bodies found in artificial blisters produced on the skin of scarlet fever patients. For the formation of the "vesicle" aqua ammoniæ fortior was employed. A piece of absorbent cotton, large enough to cover a circle 2 cm. in diameter, is saturated with the reagent and applied to a selected skin area. In from two to five minutes this is removed and the area carefully smeared with vaselin. The vesicle is formed in five to six minutes, and after the vaselin has been removed with xylol the clear fluid contents, free from red blood cells and leukocytes, is withdrawn. In this fluid "bodies" may be found which correspond exactly to the structures described by Mallory in the skin of scarlet-fever patients. The author considers these "bodies" as protozoa. They were discovered in 5 out of 18 cases of scarlet fever, but were not present in the vesicle contents of normal individuals, in the fluid from artificial vesicles produced on chemically injured skin, or in serum from artificial vesicles formed on the skin of other acute exanthemata. A full account of the work is to appear in the *Archiv f. pathologische Anatomie*.

**The Etiology of Oriental Boil.**—MARZINOWSKY and BOGROW (*Virch. Arch.*, 1904, Bd. clxxviii. p. 112), in preparations from a typical case of oriental boil, describe great numbers of small bodies which they found particularly in the epithelioid cells, less often lying free or in leukocytes, and never in red blood corpuscles. These bodies are oval or more rarely round, and measure from 1 to 3 microns in diameter. In the purulent discharge from the sores they were rarely seen, while in older or healed sores they were absent. Studied fresh and with various stains the bodies were seen to contain a small mass of chromatin; further investigations showed that the bodies divided and were motile. All attempts at cultivation were fruitless. The authors conclude that these bodies are parasites and the cause of the sores. They confirm the work of Wright, who had previously described the same bodies in a case of oriental boil. For this parasite, which they consider belongs to the class of protozoa, they propose the name of *ovoplasma orientale*. It is thought possible that the infection is conveyed by insects, since many authors have called attention to the association of mosquito bites and this affection.

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**Zonal Necrosis of the Liver.**—OPIE (*Journal of Medical Research*, July, 1904, vol. xii. p. 147) has studied the various parts of the liver lobules that may alone be affected in degenerative changes, and shows that focal necrosis may take its origin about the portal spaces at the periphery of the liver lobule when associated with eclampsia; that it may take its origin in the centre of the lobule, about the central vein, as in the hyaline necroses carefully described by Mallory, or that a mid-zonal area alone may be the seat of hyaline degeneration of the liver cells. It is with this last variety that the author particularly concerns himself. He considers that the vascular influences within the lobules are responsible for the zonal divisions, and in a series of experiments found that when foreign material reaches the liver by the portal vein it is washed from the peripheral zone by the arterial blood, and tends to be deposited in a middle zone. The author therefore thinks that toxic substances carried to the liver by the portal vein might first exert their effect upon cells within a mid-lobular zone, especially as the periphery of the lobule is perhaps less susceptible to injurious agencies on account of its arterial blood supply.

In studying the livers of five hundred autopsies, necrosis limited to a zone in the middle of the liver lobule, the outer margin of which is one-fourth to one-fifth the distance from the portal space to the central vein, and of a width equal to about one-fourth the width of the lobule, was found in nine cases. Five similar instances were found in other material.

In five cases the intermediate zone could be recognized with the naked eye. Microscopic examination usually revealed a hyaline metamorphosis of all the liver cells within this middle zone. The lesion was frequently associated with fatty degeneration, which was usually limited to the central part of the lobules, while the cells at the periphery were usually normal. Intense bacterial infection was found usually associated with this lesion.

The author considers this mid-zonal necrosis to be closely allied to acute yellow atrophy. He thinks it probable that necrosis of the middle zone of the hepatic lobule or of the combined middle and central zones



is an early stage of the process which has its termination in acute yellow atrophy. The former lesion is so frequently the result of grave infection that death follows before the secondary changes in the altered liver take place.

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**A Study of Hodgkin's Disease and its Transformation into Sarcoma.**—YAMASAKI (*Zeit. f. Heill.*, 1904, Bd. xxv. p. 269) gives the clinical histories and pathological findings of five cases of Hodgkin's disease which came to autopsy. The clinical course was characterized in all instances by a progressive anæmia resisting therapeutic measures, painless enlargement of the glands of the neck, usually by enlargement of the liver and spleen, and the lack of blood changes other than those of an anæmia. Microscopic examinations of the glandular swellings and nodules in the spleen and liver showed a new formation of connective tissue, and a marked proliferation of endothelial cells which lead to the formation of large uninuclear and multinuclear giant cells. These cells were of characteristic appearance, and were found constantly in the lymph glands and nodules from the other organs. They had no definite arrangement, but were distributed irregularly through the tissue. Neither in their appearance nor in the position of their nuclei did they possess any likeness to the Langhans giant cells of tuberculosis.

No focus of tuberculosis was found in the first two cases, except for a small healed area in a peribronchial lymph gland in the second case. In the other three cases tuberculosis of one or more organs was present. In the last case there was a general miliary tuberculosis involving the lymph glands. Inoculations of portions of glands from the non-tuberculous cases gave negative results. In the fifth case, which was complicated by miliary tuberculosis, the inoculated animals developed tuberculosis.

The author, from his observations, concludes that Hodgkin's disease is a clinical and pathological entity, and that it is distinct from tuberculosis, though patients suffering with the disease have a marked disposition for tuberculosis. He regards the condition as a peculiar chronic infection; but to show that certain cases may assume the character of a neoplasm he adds two cases to the above. In both instances the growth invaded neighboring organs and gave rise besides to secondary nodules. The histological picture was much the same as that seen in the cases of true Hodgkin's disease, the only difference being in the more cellular character of the growths. The suggestion is offered that the affection began as Hodgkin's disease and later assumed the character of a neoplasm.

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**Tuberculosis of the Bones Combined with Circulatory and Trophic Disturbances.**—Certain researches made by Herman, Kasperek and Hofbauer, and Czychlarz have pointed to the conclusion that arterial congestion, such as might be brought about by section of the abdominal sympathetic, as well as congestion followed by disturbances of nutrition, produced by section of the sciatic nerve, may favor the localization of bacteria (staphylococci, streptococci, and pneumococci), in the paws of rabbits, introduced into the circulation through the ear vein. Pétróff (*Ann. de l'Institut Pasteur*, 1904, T. xviii. p. 590) has made some experiments along these lines in regard to the localiza-

tion of tuberculous infections in the joints and long bones of rabbits. Arterial congestion of one paw of each of eleven rabbits was produced by section of the abdominal sympathetics, simple venous congestion in eight rabbits by ligature of the crural veins, and arterial congestion combined with trophic disturbances caused by section of one sciatic nerve in twelve instances. An active tuberculous virus was injected into the ear veins of these animals. In not a single instance did the above condition appear to predispose to a local infection. If tuberculosis of the bones was found it was symmetrical and bilateral. On the other hand, actual hemorrhage into the tissues with local injury seemed to play an important role in determining the seat of infection; for the thigh of one rabbit which was broken during operation showed at autopsy exquisite tuberculosis. No other joints or bones were affected. The author concludes that congestion and trophic disturbances are not of importance in the origin of local tuberculous infections of the bones and joints.

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**An Experimental Study on the Pathology of Gout.**—VAN LOGHEM, J. J. (*Ann. de l'Institut Pasteur*, 1904, T. xviii., p. 468), publishes a study on the resorption of uric acid and of sodium urate. He has employed the methods used by Freudweiler, Ilis, and others—namely, that of producing artificial tophi by injecting subcutaneously, intraperitoneally, and otherwise physiological salt solution containing small amounts of sodium urate. Injections of uric acid solutions have also been made. The observations of Rindfleisch and Freudweiler, concerning ingestion of the sodium urates by phagocytes, are confirmed. The author found at the site of the injection a month after the injection was made typical needle-like crystals of sodium urate and considers them due to a crystallization after the death of the cell of the sodium urate taken up during its life. A few hours after injections of uric acid crystals, sodium urate crystals were found at the site of injection. After twenty-four hours the uric acid crystals at the periphery had disappeared and were replaced by leukocytes, fibrin, and rosettes of sodium urate crystals. The author concludes that sodium urate can be easily precipitated in the form of needle-like crystals in the humors of the body containing a concentrated solution of uric acid. He found that in the frog an acid reaction was produced about a deposit of sodium urate, which he thinks aids in its solution.

Van Loghem explains the relation between trauma and severe attacks of gout in the following manner: Trauma brings to the part injured an exudate, which in gouty patients is laden with uric acid. From the uric acid so brought to the part, sodium urate is deposited, producing the severe symptoms. Influenza, bringing an exudate to the joints, may have the same effect in gouty individuals. He suggests that a study of the phagocytes produced about urates introduced in collodion sacs may be of service in the study of therapeutic measures.

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**Another Member of the Dysentery Group.**—DUVAL (*Journal of the American Medical Association*, 1904, vol. xliii. p. 381) describes an organism of the dysentery group, isolated from a fatal case of dysentery occurring in an adult, which differs in some respects from all hitherto described strains. The organism closely resembles the Flexner-Harris

strain of bacillus dysenteriae, but differs from it in its action on lactose and litmus milk. Its agglutinative properties also tend to distinguish it.

In neutral litmus milk the initial acidity is gradually lost to that in three or four days the milk regains its original blue color. This remains for four to six days, when a permanent acid reaction occurs. The agglutination reactions show that the bacillus is in all probability closely allied to bacillus typhosus. It is agglutinated by the blood of typhoid patients in high dilutions and also with the blood of rabbits immunized against bacillus typhosus. Likewise, bacillus typhosus is agglutinated by the blood of rabbits immunized against this organism. The organism appears, therefore, to produce common agglutinins with the typhoid bacillus, but its close cultural resemblance to the bacillus dysenteriae group serves to classify it with them.

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**The Further Differentiation of Flagellar and Somatic Agglutinins.**—In 1903 Smith and Reagh demonstrated that two different agglutinins occurred in the blood serum of rabbits immunized toward bacillus cholerae suis. When a culture of the hog-cholera bacillus belonging to the motile race was exposed to the action of serum from an animal previously inoculated with motile bacilli, it was noticed that large, loose flocculi appeared soon after beginning the experiment, whereas, if serum from a rabbit immunized toward the non-motile bacillus were mixed with this motile culture the clumps appeared fine and powdery to the naked eye and formed quite slowly. It was subsequently demonstrated that the loose flocculi were produced by a flagellar agglutinin, while the fine clumps were attributed to a somatic or body agglutinin. The separation of these substances was effected by means of absorption experiments.

BEYER and REAGH (*Journal of Medical Research*, 1904, vol. xii. p. 313) have been able to differentiate these two types of agglutinins and agglutinable substances of the hog-cholera bacillus by heat. They find that a temperature of 70° C., acting for at least twenty minutes impairs the somatic agglutinin of the serum and the flagellar substance of the bacillus, while the same temperature acting for the same time leaves nearly intact the flagellar agglutinin of the serum and the somatic agglutinable substances of the bacilli. This temperature which is sufficient to destroy the agglutinating power of motile hog-cholera bacilli does not, however, affect their power of generating the flagellar agglutinin in the animal body.

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